



STIC Search Report

Biotech-Chem Library

STIC Database Tracking Number: 125225

TO: Binta M Robinson
Location: REM 5A20
Art Unit: 1625
June 21, 2004

Case Serial Number: 10/670182

From: P. Sheppard
Location: Remsen Building
Phone: (571) 272-2529

sheppard@uspto.gov

Search Notes

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Binta Robinson Examiner #: 76704 Date: _____
Art Unit: 1025 Phone Number: 301-571272 Serial Number: 10670182
Mail Box and Bldg/Room Location: Remsen 5A20 0692 Results Format Preferred (check): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

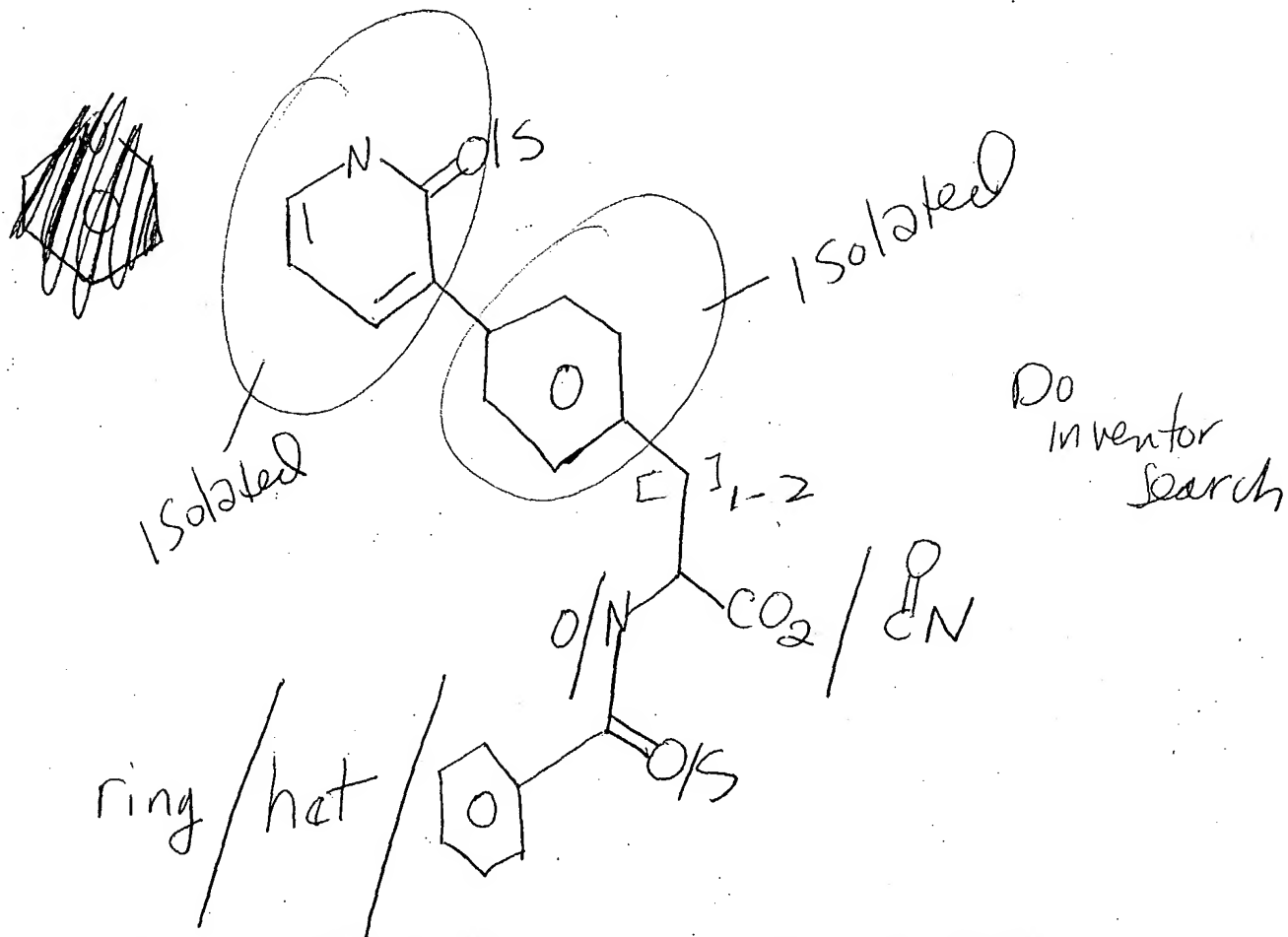
Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples of relevant citations, authors, etc., if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: _____

Inventors (please provide full names): KAPLAN ET. AL.

Earliest Priority Filing Date: _____

For Sequence Searches Only Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.



STAFF USE ONLY

Searcher: Sheppard

Type of Search

Vendors and cost where applicable

NA Sequence (#)

STN

Searcher Phone #

=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 17:46:22 ON 21 JUN 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

Copyright of the articles to which records in this database refer is held by the publishers listed in the PUBLISHER (PB) field (available for records published or updated in Chemical Abstracts after December 26, 1996), unless otherwise indicated in the original publications. The CA Lexicon is the copyrighted intellectual property of the the American Chemical Society and is provided to assist you in searching databases on STN. Any dissemination, distribution, copying, or storing of this information, without the prior written consent of CAS, is strictly prohibited.

FILE COVERS 1907 - 21 Jun 2004 VOL 140 ISS 26
FILE LAST UPDATED: 20 Jun 2004 (20040620/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=>
=>

=> d his 118

(FILE 'HCAPLUS' ENTERED AT 17:40:35 ON 21 JUN 2004)

E SIDDURI A/AU, IN

L18 18 S E5-E8

=>
=>

=> d ibib abs 118 1-18

L18 ANSWER 1 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:585056 HCAPLUS

DOCUMENT NUMBER: 138:214843

TITLE: N-Aroyl-l-Phenylalanine Derivatives as VCAM/VLA-4 Antagonists

AUTHOR(S): Sidduri, Achyutharao; Tilley, Jefferson W.;
Lou, Jian Ping; Chen, Li; Kaplan, Gerry; Mennona,
Frank; Campbell, Robert; Guthrie, Robert; Huang,
Tai-Nan; Rowan, Karen; Schwinge, Virginia; Renzetti,
Louis M.

CORPORATE SOURCE: Roche Research Center, Hoffmann-La Roche Inc., Nutley,
NJ, 07110, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (2002),
12(17), 2479-2482

CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 138:214843

AB A series of N-benzoyl-4-[(2,6-dichlorobenzoyl)amino]-l-phenylalanine derivs. was prepared in order to optimize the substitution on the N-benzoyl moiety for VCAM/VLA-4 antagonist activity. Disubstitution in the 2- and 6-positions is favored and a range of small alkyl and halogen are tolerated. A model of the bioactive conformation of these compds. is proposed.

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 2 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:585055 HCAPLUS

DOCUMENT NUMBER: 138:214842

TITLE: N-Cycloalkanoyl-L-Phenylalanine Derivatives as
VCAM/VLA-4 Antagonists

AUTHOR(S): Sidduri, Achyutharao; Tilley, Jefferson W.;
Hull, Kenneth; Lou, Jian Ping; Kaplan, Gerry;
Sheffron, Allen; Chen, Li; Campbell, Robert; Guthrie,
Robert; Huang, Tai-Nan; Hubby, Nicholas; Rowan, Karen;
Schwinge, Virginia; Renzetti, Louis M.

CORPORATE SOURCE: Roche Research Center, Hoffmann-La Roche Inc., Nutley,
NJ, 07110, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (2002),
12(17), 2475-2478

CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 138:214842

AB A systematic structure-activity relationship investigation of the lead
compound, cycloalkanoyl phenylalanine derivative resulted the identification of
several N-[(substituted alkyl)cycloalkanoyl]-4-[(2,6-
dichlorophenyl)carbonyl]amino]-L-phenylalanine derivs. as potent
VCAM/VLA-4 antagonists. The data are consistent with a model of these
comps. in which these alkanoylphenylalanines reside in a compact gauche
(-) bioactive conformation.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 3 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:142705 HCAPLUS

DOCUMENT NUMBER: 136:183830

TITLE: Preparation of tetrazolylphenylacetamide glucokinase
activators for treatment or prophylaxis of type II
diabetes

INVENTOR(S): Sidduri, Achyutharao

PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.

SOURCE: PCT Int. Appl., 115 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002014312	A1	20020221	WO 2001-EP9207	20010809
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 2002035266	A1	20020321	US 2001-924247	20010808
US 6369232	B2	20020409		
AU 2001083998	A5	20020225	AU 2001-83998	20010809
EP 1311504	A1	20030521	EP 2001-962926	20010809

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

BR 2001013312	A	20030701	BR 2001-13312	20010809
JP 2004506632	T2	20040304	JP 2002-519452	20010809
US 2002035267	A1	20020321	US 2001-975713	20011011
US 6388088	B2	20020514		
US 2002065275	A1	20020530	US 2002-50508	20020116
US 6441180	B2	20020827		

PRIORITY APPLN. INFO.:

US 2000-225494P	P	20000815
US 2001-924247	A3	20010808
WO 2001-EP9207	W	20010809
US 2001-975713	A3	20011011

OTHER SOURCE(S): MARPAT 136:183830

AB Tetrazolylphenylacetamides, 4-R1-3-R2C6H3ZC(O)NHR4 (I; e.g. N-(5-bromopyridin-2-yl)-3-cyclopentyl-2-[3-chloro-4-(5-methyltetrazol-1-yl)phenyl]propionamide (1); Z is (E)-R3(CH2)nCH:C< or R3(CH2)nCH2C*H<; the asterisk denotes an asym. C; 1 of R1 or R2 is 5-R5-1H-tetrazol-1-yl and the other is H, halogen, lower alkyl sulfonyl, perfluoro lower alkyl, cyano, or nitro; R3 is cycloalkyl; R4 is -C(O)-NHR6 or a five- or six-membered heteroarom. ring connected by a ring C atom to the amide group; R5 is lower alkyl, perfluoro lower alkyl; R6 = H, lower alkyl; n = 0, 1), are active as glucokinase activators, and are able to increase insulin secretion, which makes them useful for treating type II diabetes. In the in vitro glucokinase assay, all I described in the synthesis examples had an $SCl.5 \leq 30 \mu M$. Nine I (e.g. 1) have excellent glucokinase activating activity in vivo when administered orally in accordance with the procedure described. 22 Example preps. are given. For example, a solution of PPh3 (0.9 mmol) in CH2Cl2 (6 mL) was cooled to 0° and then treated with N-bromosuccinimide (0.9 mmol). The reaction mixture was stirred at 0° for 30 min and then treated with 2-[3-chloro-4-(5-methyltetrazol-1-yl)phenyl]-3-cyclopentylpropionic acid (2; 0.45 mmol). The clear solution was stirred for 15 min at 0° and then allowed to warm to 25° where it was stirred for 2 h. The reaction mixture was then treated with 2-amino-5-bromopyridine (1.35 mmol), and the resulting suspension was stirred for 2 d at 25°. After workup, 42% of 1 was obtained as an amorphous white solid. To prepare intermediate 2, activated Zn dust suspension (10 mmol) in THF was treated with trimethylsilyl chloride (1 mmol), and the suspension was stirred for 15 min at 25°. The reaction mixture was then treated dropwise with a solution of (E)-3-cyclopentyl-2-iodoacrylic acid Me ester (preparation given; 4.5 mmol) in dry THF (2 mL) over 3 min. The reaction mixture was then stirred at 40-45° for 1 h and then stirred overnight at 25°. The reaction mixture was then diluted with dry THF (3 mL), and the stirring was stopped to allow the excess Zn dust to settle down (.apprx.2 h). In a sep. reaction flask, bis(dibenzylideneacetone)palladium(0) (0.1 mmol) and PPh3 (0.4 mmol) in dry THF (4 mL) was stirred at 25° under Ar for 10 min and then treated with 1-(2-chloro-4-iodophenyl)-5-methyl-1H-tetrazole (preparation given; 2.73 mmol) and the freshly prepared Zn compound in THF. The resulting brick red solution was stirred at 25° over the weekend and then heated at 40-45° for 4 h. Workup gave 91% (E)-2-[3-chloro-4-(5-methyltetrazol-1-yl)phenyl]-3-cyclopentylacrylic acid Me ester (3). A solution of Ni(II) chloride hexahydrate (0.8 mmol) and 3 (2.0 mmol) in MeOH (15 mL) was cooled to 0° and then treated with NaBH4 (12 mmol) in five portions. After the addition, the black reaction mixture was stirred for 15 min at 0° and then allowed to warm to 25° where it was stirred for 2 d. Workup gave 99% racemic 2-[3-chloro-4-(5-methyltetrazol-1-yl)phenyl]-3-cyclopentylpropionic acid Me ester (4). A solution of 4 (2.0 mmol) in EtOH (20 mL) was treated with a 1 N aqueous NaOH solution (4 mL). The solution was heated at 45-50° for 3 h, at which time, thin layer chromatog. anal. of the reaction mixture indicated the absence of starting material. Workup gave 90% 2.

REFERENCE COUNT:

3

THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 4 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:41809 HCAPLUS
DOCUMENT NUMBER: 137:149523
TITLE: VLA-4 antagonists
AUTHOR(S): Tilley, Jefferson W.; **Sidduri, Achyutharao**
CORPORATE SOURCE: Roche Research Center, Hoffmann-La Roche, Inc.,
Nutley, NJ, 07110, USA
SOURCE: Drugs of the Future (2001), 26(10), 985-998
CODEN: DRFUD4; ISSN: 0377-8282
PUBLISHER: Prous Science
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review on the role of VLA-4/VCAM-1 (very late activating antigen-4/vascular cell adhesion mol.-1) inhibitors with and without concomitant inhibition of $\alpha 4\beta 7$ -mediated interactions in the treatment of various human inflammatory diseases. Such inhibitors include cyclic peptide derivs., linear peptides as LDV mimics and acylphenylalanines.

REFERENCE COUNT: 114 THERE ARE 114 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 5 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:872129 HCAPLUS
DOCUMENT NUMBER: 136:200445
TITLE: Synthesis of constrained L-phenylalanine derivatives incorporating a benzazepinone or an azepinone ring as VCAM/VLA-4 antagonists
AUTHOR(S): **Sidduri, Achyutharao**; Lou, Jian Ping;
Campbell, Robert; Rowan, Karen; Tilley, Jefferson W.
CORPORATE SOURCE: Hoffmann-La Roche Inc., Roche Research Center, Nutley, NJ, 07110, USA
SOURCE: Tetrahedron Letters (2001), 42(50), 8757-8760
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 136:200445
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Novel constrained L-phenylalanines such as benzazepinone derivative I and spiro(azepinone-cyclopentane) derivative II, were synthesized in 13 and 8 steps, resp., employing a key base-catalyzed intramol. cyclization reaction. I was comparable in potency in a VCAM/VLA-4 ELISA assay to the corresponding unconstrained N-(dimethylbenzoyl)phenylalanine derivative III suggesting that cyclization favored the bioactive conformation. However, II was 100-fold less potent than the corresponding unconstrained N-[(methoxyethyl)cyclopentanoyl]phenylalanine derivative IV.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

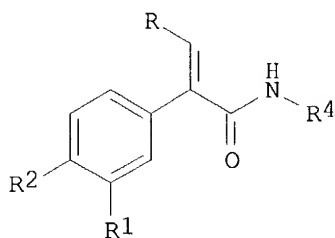
L18 ANSWER 6 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:453042 HCAPLUS
DOCUMENT NUMBER: 135:61317
TITLE: Preparation of (E)-2,3-disubstituted-N-thiazolylacrylamides and related compounds as glucokinase activators

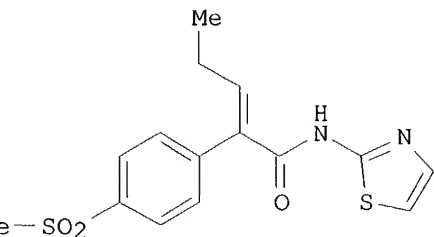
INVENTOR(S): Corbett, Wendy Lea; Sarabu, Ramakanth; **Sidduri, Achyutharao**
 PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.
 SOURCE: PCT Int. Appl., 93 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001044216	A1	20010621	WO 2000-EP12612	20001212
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6353111	B1	20020305	US 2000-727624	20001201
BR 2000016392	A	20020827	BR 2000-16392	20001212
EP 1242397	A1	20020925	EP 2000-987392	20001212
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003516980	T2	20030520	JP 2001-544706	20001212
NO 2002002863	A	20020614	NO 2002-2863	20020614
PRIORITY APPLN. INFO.:				
			US 1999-170783P	P 19991215
			US 1999-170786P	P 19991215
			WO 2000-EP12612	W 20001212

OTHER SOURCE(S): MARPAT 135:61317



I



II

B The title 2,3-disubstituted trans olefinic N-heteroarom. or ureido propenamides (I) [wherein R1 and R2 = independently H, halo, NH2, NO2, (perfluoro)alkyl, alkylthio, alkylsulfonyl(methyl),

perfluoroalkylsulfonyl, or alkylsulfinyl; R = (CH₂)_mR₃; R₃ = cycloalkyl; R₄ = CONHR₇, (mono)substituted 5- or 6-membered heteroarom. ring, or (CH₂)_nCOOR₇; m = 0-1; n = 0-4; R₇ = H or alkyl; olefinic double bond is trans] were prepared as glucokinase activators, which increase insulin secretion in the treatment of type II diabetes (no data). For example, Grignard addition of EtMgBr to Me propiolate and treatment with I₂ gave the 2-iodopentenoate (67%). Zinc catalyzed addition of 4-bromophenyl Me sulfone to the 2-iodopentenoate (78%), deesterification with aqueous NaOH (82%), and amidation with 2-aminothiazole (16%) afforded II. All of the example compds. activated glucokinase in vitro with SC_{1.5} ≤ 30 μM.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 7 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:435056 HCAPLUS

DOCUMENT NUMBER: 135:33648

TITLE: Synthesis of 4-pyrimidinyl-N-acyl-L-phenylalanine derivatives for use as vascular cell adhesion molecule-1 (VCAM-1) binding inhibitors

INVENTOR(S): Sidduri, Achyutharao; Tilley, Jefferson Wright

PATENT ASSIGNEE(S): F. Hoffmann-La Roche Ag, Switz.

SOURCE: PCT Int. Appl., 118 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

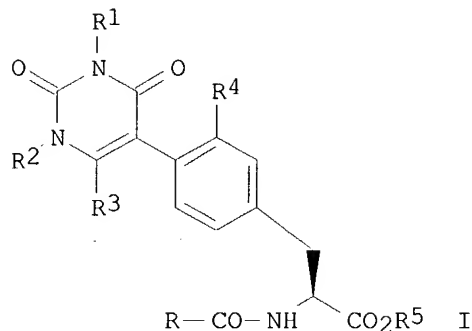
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001042225	A2	20010614	WO 2000-EP11884	20001128
WO 2001042225	A3	20020221		
W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
US 6380387	B1	20020430	US 2000-717912	20001121
BR 2000016195	A	20020813	BR 2000-16195	20001128
EP 1237878	A2	20020911	EP 2000-989906	20001128
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
JP 2003516396	T2	20030513	JP 2001-543526	20001128
NZ 518828	A	20040326	NZ 2000-518828	20001128
ZA 2002003533	A	20030804	ZA 2002-3533	20020503
NO 2002002633	A	20020604	NO 2002-2633	20020604

PRIORITY APPLN. INFO.: US 1999-169089P P 19991206
US 2000-245601P P 20001103
WO 2000-EP11884 W 20001128

OTHER SOURCE(S): MARPAT 135:33648

GI



AB Title compds. [(I); R = substituted Ph, heterocycle; R1, R2, R3 = (independently) H, (substituted)alkyl, arylalkyl, aryl; R4 = H, alkyl, Cl, alkoxy; R5 = H, (substituted)alkyl, OC(O)alkyl] were prepared and tested for biol. activity as vascular cell adhesion mol.-1 (VCAM-1) binding inhibitors for use in treating asthma, inflammatory bowel disease, multiple sclerosis, or rheumatoid arthritis. Thus, 1,3-dimethyl-5-iodouracil (preparation given) was reacted with N-[(1,1-dimethylethoxy)carbonyl]-4-iodo-L-phenylalanine Me ester, the product then N-deprotected and reacted with 2-chloro-6-methylbenzoic acid, followed by deesterification to give I [R = 2-Cl-6-Me-C6H4; R1, R2 = Me; R3, R4, R5 = H (II)]. In in vitro tests for activity in VCAM/VLA-4 (ELISA OR Ramos Cell Assay), II had IC50 values of <10 nM and < 100 nM, resp.

L18 ANSWER 8 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:435046 HCAPLUS

DOCUMENT NUMBER: 135:33647

TITLE: Preparation of pyridinyl phenylalanine derivatives

INVENTOR(S): Kaplan, Gerald Lewis; **Sidduri, Achyutharao;**

Tilley, Jefferson Wright

PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.

SOURCE: PCT Int. Appl., 97 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001042215	A1	20010614	WO 2000-EP11979	20001129
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6388084	B1	20020514	US 2000-717684	20001121
BR 2000016172	A	20020820	BR 2000-16172	20001129
EP 1244625	A1	20021002	EP 2000-985117	20001129
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003516392	T2	20030513	JP 2001-543516	20001129
NZ 518888	A	20040227	NZ 2000-518888	20001129
US 2002133015	A1	20020919	US 2002-59618	20020129

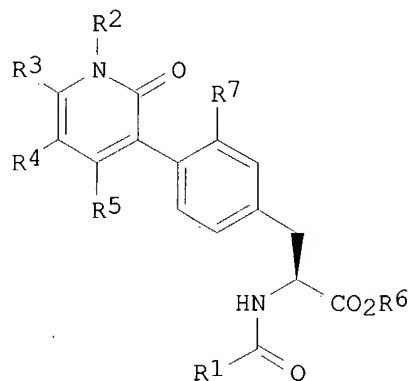
NO 2002002650
PRIORITY APPLN. INFO.:

A 20020605

NO 2002-2650
US 1999-169090P P 19991206
US 2000-245603P P 20001103
US 2000-717684 A3 20001121
WO 2000-EP11979 W 20001129

OTHER SOURCE(S):
GI

MARPAT 135:33647



I

AB Pyridinyl phenylalanine derivs. I (R1 = substituted aryl, substituted 5 or 6 membered heteroarom. ring containing N, O and S bonded via a carbon atom to the amide carbonyl, 3-7 membered ring substituted with alkyl, alkenyl, fluoroalkenyl, arylalkyl, heteroarylalkyl, azidoalkyl, cyanoalkyl, hydroxyalkyl, alkyl sulfonyl, alkyl sulfinyl; R2 = H, (un)substituted alkyl, aryl, or arylalkyl; R3 = H, halogen, alkyl, trifluoromethyl, or aryl; R4 = H, halogen, alkyl, or aryl; R5 = H, alkyl, alkoxy, trifluoromethyl, or aryl; R6 = H, alkyl, alkylcarbonyloxy, substituted aminoalkyl, substituted heterocyclylalkyl; R7 = H, Cl, alkoxy, or alkyl) were prepared as inhibitors of the binding of VCAM-1 to VLA-4 and are useful in treating chronic inflammatory diseases. Thus, N-[(2-chloro-6-methylphenyl)carbonyl]-4-(5-chloro-1-methyl-2-oxo-3-pyridinyl)-L-phenylalanine (II) was prepared from N-[(1,1-dimethylethoxy)carbonyl]-4-iodo-L-phenylalanine Me ester in 5 steps via palladium catalyzed reaction with 3-bromo-5-chloro-1-methyl-2-pyridinone and coupling with 2-chloro-6-methylbenzoic acid. II showed antiinflammatory activity in vitro in the VCAM/VLA-4 screening assay (IC50 < 1 nM).

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 9 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:592696 HCAPLUS

DOCUMENT NUMBER: 133:177488

TITLE: Preparation of phenylalanine thioamide derivatives

INVENTOR(S): Hull, Kenneth Gregory; Sidduri, Achytharao; Tilley, Jefferson Wright

PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.

SOURCE: PCT Int. Appl., 106 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

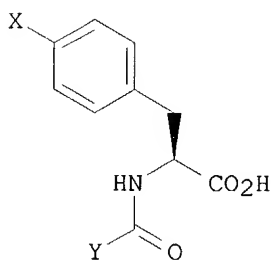
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
------------	------	------	-----------------	------

WO 2000048994	A1	20000824	WO 2000-EP1058	20000210
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
BR 2000008280	A	20011106	BR 2000-8280	20000210
EP 1154993	A1	20011121	EP 2000-903680	20000210
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
TR 200102399	T2	20020121	TR 2001-200102399	20000210
JP 2002537286	T2	20021105	JP 2000-599735	20000210
NZ 513254	A	20031031	NZ 2000-513254	20000210
US 6288267	B1	20010911	US 2000-505903	20000217
US 2002028933	A1	20020307	US 2001-812325	20010320
US 2001041799	A1	20011115	US 2001-863579	20010523
US 6458844	B2	20021001		
US 2002010338	A1	20020124	US 2001-863567	20010523
US 6479666	B2	20021112		
US 2002040148	A1	20020404	US 2001-864032	20010523
US 6426348	B2	20020730		
US 2002052508	A1	20020502	US 2001-864104	20010523
US 6423728	B2	20020723		
ZA 2001006180	A	20021028	ZA 2001-6180	20010726
HR 2001000595	A1	20020831	HR 2001-595	20010810
NO 2001004018	A	20010817	NO 2001-4018	20010817
PRIORITY APPLN. INFO.:			US 1999-120475P	P 19990218
			US 1998-137798	A 19980821
			US 1998-138353	A 19980821
			WO 2000-EP1058	W 20000210
			US 2000-505903	A3 20000217
OTHER SOURCE(S):			MARPAT 133:177488	
GI				



AB Phenylalanine thioamide derivs. I [X = substituted benzoylamino or Het-CONH (Het is a 5- or 6-membered heteroarom. ring containing 1-3 heteroatoms (N, O, S) or a 9- or 10-membered bicyclic heteroarom. ring containing 1-4 heteroatoms), 5-oxo-1-imidazolidinyl substituted at C(2) by aryl, heteroaryl, arylalkyl, heteroarylalkyl, at C(4) by (un)substituted alkyl, aryl, heteroaryl, arylalkyl, or heteroarylalkyl, and at N(3) by (un)substituted alkanoyl or aroyl; Y = (un)substituted Ph, substituted heteroaryl or heterocyclyl] were prepared as inhibitors of the binding of VCAM-1 to VLA-4 and are useful in treating inflammation associated with

chronic diseases such as rheumatoid arthritis, multiple sclerosis, asthma, and inflammatory bowel disease. Thus, 4-[[[(2,6-dichlorophenyl)carbonyl]amino]-N-[[1-(2-methoxyethyl)cyclopentyl]thioxomethyl]-L-phenylalanine was prepared from N-[[1-(2-methoxyethyl)cyclopentyl]carbonyl]-4-nitro-L-phenylalanine Me ester by sulfuration with Lawesson's reagent, nitro group reduction with zinc dust, acylation with 2,6-dichlorobenzoyl chloride, and saponification and showed IC50 = 4.0 nM and 66.5 nM in the VLA-4/VCAM-1 and Ramos (VLA-4)/VCAM-1 screening assays.

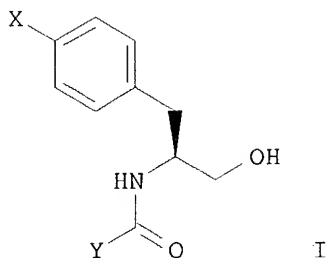
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 10 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:592690 HCAPLUS
DOCUMENT NUMBER: 133:177487
TITLE: Preparation of phenylalaninol derivatives
INVENTOR(S): Sidduri, Achytharao; Tilley, Jefferson Wright
PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.
SOURCE: PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000048988	A1	20000824	WO 2000-EP1168	20000212
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
BR 2000008368	A	20011106	BR 2000-8368	20000212
EP 1154987	A1	20011121	EP 2000-903692	20000212
EP 1154987	B1	20040421		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
TR 200102395	T2	20011221	TR 2001-200102395	20000212
JP 2002537283	T2	20021105	JP 2000-599729	20000212
US 6420600	B1	20020716	US 2000-506062	20000217
ZA 2001006075	A	20021024	ZA 2001-6075	20010724
HR 2001000594	A1	20020831	HR 2001-594	20010810
NO 2001003946	A	20010814	NO 2001-3946	20010814
PRIORITY APPLN. INFO.: US 1999-120498P P 19990218				
WO 2000-EP1168 W 20000212				

OTHER SOURCE(S): MARPAT 133:177487
GI



AB Phenylalaninol derivs. I [X = substituted benzoylamino or Het-CONH (Het is a 5- or 6-membered heteroarom. ring containing 1-3 heteroatoms (N, O, S) or a 9- or 10-membered bicyclic heteroarom. ring containing 1-4 heteroatoms), 5-oxo-1-imidazolidinyl substituted at C(2) by aryl or heteroaryl, at C(4) by (un)substituted alkyl, aryl, heteroaryl, arylalkyl, or heteroarylalkyl, and at N(3) by (un)substituted alkanoyl or aroyl; Y = (un)substituted Ph, substituted heteroaryl or heterocyclyl] were prepared as effective inhibitors of the binding of VCAM-1 to VLA-4 in vivo and are useful in treating inflammation in inflammatory diseases in which such binding acts to bring on the inflammation. Thus, 4-[[2,6-dichlorophenyl)carbonyl]amino]-N-[(2-chloro-6-methylphenyl)carbonyl]-L-phenylalaninol, prepared by borohydride reduction of the Me ester, caused a significant decrease in the number and percent of inflammatory cells present in the lavage fluid relative to vehicle treated control animals.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 11 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:364687 HCAPLUS

DOCUMENT NUMBER: 133:164252

TITLE: An unusual solvent effect on the regiochemical outcome (N-9 versus N-7) of guanine glycosylation using Robins' reagent (2-N-acetyl-6-O-diphenylcarbamoylguanine)

AUTHOR(S): Cheung, Adrian Wai-Hing; Sidduri, Achyutharao ; Garofalo, Lisa M.; Goodnow, Robert A., Jr.

CORPORATE SOURCE: Roche Research Center, Hoffmann-La Roche Inc., Nutley, NJ, 07110, USA

SOURCE: Tetrahedron Letters (2000), 41(18), 3303-3307
CODEN: TELEAY; ISSN: 0040-4039

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 133:164252

AB An unexpectedly low N-9/N-7 regioselectivity was obtained when Robins' reagent (2-N-acetyl-6-O-diphenylcarbamoylguanine) was coupled with a D-glucosamine derivative under trimethylsilyl trifluoromethanesulfonate activation. An unprecedented solvent effect (toluene vs. dichloroethane) on the N-9/N-7 ratio was also observed in the same study. The use of 2-N-acetyl-6-O-benzylguanine to successfully overcome the above regioselectivity problem is described.

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 12 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:166589 HCAPLUS

DOCUMENT NUMBER: 130:209978

TITLE: Preparation of N-aroylphenylalanine derivatives as vascular cell adhesion molecule-1 (VCAM-1) binding inhibitors

INVENTOR(S): Chen, Li; Guthrie, Robert William; Huang, Tai-Nang;
Hull, Kenneth G.; **Sidduri, Achytharao;**
Tilley, Jefferson Wright
PATENT ASSIGNEE(S): F.Hoffmann-La Roche A.-G., Switz.
SOURCE: PCT Int. Appl., 215 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9910313	A1	19990304	WO 1998-EP5144	19980813
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2300121	AA	19990304	CA 1998-2300121	19980813
AU 9893419	A1	19990316	AU 1998-93419	19980813
AU 742928	B2	20020117		
EP 1005446	A1	20000607	EP 1998-946326	19980813
EP 1005446	B1	20040225		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
TR 200000481	T2	20000621	TR 2000-200000481	19980813
BR 9811988	A	20000905	BR 1998-11988	19980813
JP 2001514163	T2	20010911	JP 2000-507644	19980813
ZA 9807602	A	19990504	ZA 1998-7602	19980821
US 6455550	B1	20020924	US 1998-138353	19980821
TW 515792	B	20030101	TW 1998-87113767	19980821
US 2003109459	A1	20030612	US 2002-117616	20020405
PRIORITY APPLN. INFO.:			US 1997-56929P	P 19970822
			US 1998-94591P	P 19980729
			WO 1998-EP5144	W 19980813
			US 1998-138353	B3 19980821
OTHER SOURCE(S):		MARPAT 130:209978		
GI				

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [one of X, X1 = H, halo, lower alkyl and the other = (un)substituted group X6, X7, X10; R1 = H, lower alkyl; n = 0, 1; Het = 5-6 membered heteroarom. ring containing 1-3 heteroatoms N, O, S, or 9-10 membered bicyclic heteroarom. ring containing 1-4 heteroatoms N, O, S; R19 = (un)substituted lower alkyl, aryl, heteroaryl, arylalkyl, heteroarylalkyl; R18 = H, any group R19; R20 = (un)substituted lower alkyl, aroyl, lower alkanoyl; Y = CR22R23R24, 3-7 membered ring Y2; R22, R23 = (un)substituted aryl, heteroaryl, lower alkyl; R24 = H, CN, (un)substituted aryl, lower alkyl, with provisos; R25 = lower alkyl, F-(un)substituted lower alkenyl, R26(CH2)m; R26 = aryl, heteroaryl, N3, CN, OH, NO2, amino, lower alkoxy, lower alkoxy carbonyl, lower alkanoyl, lower alkylthio, lower alkylsulfonyl, lower alkylsulfinyl, etc.; Q = bond, (CH2)pO, (CH2)pS, (CH2)p; m = 0-4; p = 0-3; Z = H, lower alkyl] and pharmaceutically acceptable salts and esters thereof, are disclosed which have activity as inhibitors of binding between VCAM-1 and cells expressing integrin VLA-4. Such compds. are useful for treating diseases whose symptoms and /or

damage are related to the binding of VCAM-1 to cells expressing VLA-4. Thus, amidation of 4-amino-N-[(1-phenylcyclopentyl)carbonyl]-L-phenylalanine Me ester (preparation given) with 4-quinolinecarboxylic acid and saponification gave desired title derivative II as its sodium salt. II inhibited VLA-4 binding to immobilized VCAM-1 with IC50 = 2.7 nM in solid-phase dual antibody assay.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 13 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:166588 HCAPLUS

DOCUMENT NUMBER: 130:196952

TITLE: Preparation of N-alkanoylphenylalanine derivatives as vascular cell adhesion molecule-1 (VCAM-1) binding inhibitors

INVENTOR(S): Chen, Li; Guthrie, Robert William; Huang, Tai-Nang; Hull, Kenneth G.; Sidduri, Achyutharao; Tilley, Jefferson Wright

PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.

SOURCE: PCT Int. Appl., 135 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9910312	A1	19990304	WO 1998-EP5135	19980813
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
CA 2301377	AA	19990304	CA 1998-2301377	19980813
AU 9892620	A1	19990316	AU 1998-92620	19980813
AU 739511	B2	20011011		
EP 1005445	A1	20000607	EP 1998-945235	19980813
EP 1005445	B1	20040526		
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			
TR 200000482	T2	20000621	TR 2000-200000482	19980813
BR 9811730	A	20000905	BR 1998-11730	19980813
JP 2001514162	T2	20010911	JP 2000-507643	19980813
NZ 502813	A	20021025	NZ 1998-502813	19980813
RU 2220950	C2	20040110	RU 2000-106434	19980813
EP 1403247	A1	20040331	EP 2003-27533	19980813
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY			
ZA 9807604	A	19990518	ZA 1998-7604	19980821
US 6229011	B1	20010508	US 1998-137798	19980821
TW 490458	B	20020611	TW 1998-87113768	19980821
HR 2000000080	A1	20001231	HR 2000-80	20000211
NO 2000000841	A	20000221	NO 2000-841	20000221
PRIORITY APPLN. INFO.:			US 1997-56718P	P 19970822
			US 1998-94592P	P 19980729
			EP 1998-945235	A3 19980813
			WO 1998-EP5135	W 19980813

OTHER SOURCE(S): MARPAT 130:196952

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [one of X, X1 = H, halo, lower alkyl and the other = (un)substituted group X6, X7, X10; R1 = H, lower alkyl; n = 0, 1; Het = 5-6 membered heteroarom. ring containing 1-3 heteroatoms N, O, S, or 9-10 membered bicyclic heteroarom. ring containing 1-4 heteroatoms N, O, S; R18 = lower alkyl, aryl, heteroaryl, arylalkyl, heteroarylalkyl; R19 = (un)substituted lower alkyl, aryl, heteroaryl; R20 = lower alkyl, lower alkanoyl; R19R20 = (CH₂)₄; Y = group Y1, (un)substituted 5-6 membered monocyclic heteroarom. group containing 1-3 heteroatoms N, O, S, 9-10 membered bicyclic heteroarom. group containing 1-4 heteroatoms N, O, S; R22, R23 = H, lower alkyl, lower alkoxy, lower alkoxyaryl, lower alkylamino, aryl, arylalkyl, NO₂, CN, lower alkylthio, lower alkylsulfinyl, lower alkylsulfonyl, lower alkanoyl, halo, perfluoroalkyl; both R22 and R23 ≠ H; R24 = H, OH, lower alkyl, lower alkoxy, lower alkylsulfonyl, amino, aryl, NO₂, CN, halo, (un)substituted 1-amino-5-tetrazolyl, sulfonamido, carboxamido; R22R24 = fused benzene ring; Z = H, lower alkyl; R31 = H, (un)substituted lower alkyl] and pharmaceutically acceptable salts and esters thereof, are disclosed which have activity as inhibitors of binding between VCAM-1 and cells expressing integrin VLA-4. Such compds. are useful for treating diseases whose symptoms and/or damage are related to the binding of VCAM-1 to cells expressing VLA-4. Thus, amidation of 4-amino-N-tert-butoxycarbonyl-L-phenylalanine Me ester with 2,6-dichlorobenzoyl chloride, followed by acidic deprotection, amidation with 2-chloro-6-methylbenzoic acid, and saponification gave desired title derivative II. II inhibited VLA-4 binding to immobilized VCAM-1 with IC₅₀ = 0.33 nM in solid-phase dual antibody assay.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 14 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1993:448724 HCAPLUS

DOCUMENT NUMBER: 119:48724

TITLE: Selective mono- and polymethylene homologations of copper reagents using (iodomethyl)zinc iodide

AUTHOR(S): Sidduri, AchyuthaRao; Rozema, Michael J.; Knochel, Paul

CORPORATE SOURCE: Dep. Chem., Univ. Michigan, Ann Arbor, MI, 48109-1055, USA

SOURCE: Journal of Organic Chemistry (1993), 58(10), 2694-713
CODEN: JOCEAH; ISSN: 0022-3263

DOCUMENT TYPE: Journal

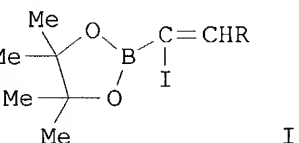
LANGUAGE: English

OTHER SOURCE(S): CASREACT 119:48724

AB A wide range of unsatd. aryl-, alkenyl-, and alkynylcopper compds. can be selectively homologated by a methylene unit using (iodomethyl)zinc iodide or bis(iodomethyl)zinc. These reactions allow the generation of mixed allylic zinc-copper compds. which can be efficiently trapped with carbonyl compds. An application to a general preparation of functionalized α -methylene- γ -butyrolactones is described. The homologation of alkynylcoppers with (iodomethyl)zinc iodide allows a one-pot preparation of propargylic copper reagents which in the presence of a carbonyl compound provide various homopropargylic alcs. in excellent yields. In the absence of an electrophile, a clean quadruple methylene homologation of alkynylcopper occurs to furnish dienic copper reagents. The homologation of other types of copper reagents is also possible, and carbanions at the α -position to amines as well as homoenolates of aldehydes or ketones can also be prepared by this method.

18 ANSWER 15 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 1993:147206 HCAPLUS
 DOCUMENT NUMBER: 118:147206
 TITLE: Preparation of highly functionalized 3,4-disubstituted cyclobutene-1,2-diones using functionalized zinc-copper organometallics
 AUTHOR(S): **Sidduri, AchyuthaRao**; Budries, Nicole; Laine, Richard M.; Knochel, Paul
 CORPORATE SOURCE: Dep. Chem., Univ. Michigan, Ann Arbor, MI, 48109, USA
 SOURCE: Tetrahedron Letters (1992), 33(49), 7515-18
 CODEN: TELEAY; ISSN: 0040-4039
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 118:147206
 AB Selective substitution reactions of zinc-copper reagents with 3,4-dichlorocyclobutene-1,2-dione facilitate the preparation of a variety of new, functionalized sym. and mixed 2,4-disubstituted cyclobutene-1,2-diones.

18 ANSWER 16 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 1992:571511 HCAPLUS
 DOCUMENT NUMBER: 117:171511
 TITLE: Preparation and reactions of 1,1-zinc, boron and 1,1-copper, boron alkenyl bimetallics
 AUTHOR(S): Waas, Jack R.; **Sidduri, AchyuthaRao**; Knochel, Paul
 CORPORATE SOURCE: Dep. Chem., Univ. Michigan, Ann Arbor, MI, 48109, USA
 SOURCE: Tetrahedron Letters (1992), 33(26), 3717-20
 CODEN: TELEAY; ISSN: 0040-4039
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 117:171511
 GI



AB Pinacol α -iodoalkenylboronates [I, R = Bu, isopentyl, (CH₂)₃Cl] readily prepared by the hydroboration of 1-iodoalkynes, were converted to 1,1-bimetallics of boron and zinc or copper which react with a wide range of electrophiles affording polyfunctional boronic esters. After H₂O₂ oxidation, polyfunctional ketones were produced in good to excellent yields.

18 ANSWER 17 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 1992:531003 HCAPLUS
 DOCUMENT NUMBER: 117:131003
 TITLE: New preparation of α -methylene- γ -butyrolactones mediated by (iodomethyl)zinc iodide
 AUTHOR(S): **Sidduri, AchyuthaRao**; Knochel, Paul
 CORPORATE SOURCE: Dep. Chem., Univ. Michigan, Ann Arbor, MI, 48109, USA
 SOURCE: Journal of the American Chemical Society (1992), 114(19), 7579-81
 CODEN: JACSAT; ISSN: 0002-7863
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 117:131003
 AB The addition of polyfunctional zinc-copper reagents FG-RCu(CN)ZnI (RG-R =

functional group) to Et propiolate or di-Et acetylenedicarboxylate provides highly functionalized α -carbethoxyalkenyl organometallics which are cleanly homologated in the presence of an aldehyde or ketone by a methylene unit using iodomethylzinc iodide and converted to an intermediate allylic copper-zinc reagent. Their reaction with the carbonyl functionality gives, after work-up, highly functionalized α -methylene- γ -butyrolactones in good yields. The reaction proceeds stereoselectively affording preferentially cis 4,5-disubstituted lactones as proved by NMR-spectroscopy and x-ray anal.

L18 ANSWER 18 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1992:150845 HCAPLUS

DOCUMENT NUMBER: 116:150845

TITLE: Preparation of functionalized dialkylzinc reagents via an iodine-zinc exchange reaction. Highly enantioselective synthesis of functionalized secondary alcohols

AUTHOR(S): Rozema, Michael J.; Sidduri, AchyuthaRao; Knochel, Paul

CORPORATE SOURCE: Dep. Chem., Univ. Michigan, Ann Arbor, MI, 48109-1055, USA

SOURCE: Journal of Organic Chemistry (1992), 57(7), 1956-8
CODEN: JOCEAH; ISSN: 0022-3263

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 116:150845

AB The treatment of primary iodides, FG-RI, with 3-5 equiv diethylzinc without solvent at 44-55° for 1-20 h affords, after the vacuum removal of the excess diethylzinc, dialkylzincs (FG-R)₂Zn in excellent yields (ca. 85-90%). Remarkably, this iodine-zinc exchange reaction is compatible with the presence of functional groups such as an ester, nitrile, chloride or boronic ester group. After the addition of CuCN·2LiCl, new organocopper reagents, FG-RCu(CN)Zn(FG-R), are formed. They react in high yields with a wide range of electrophiles (allylic and alkynyl halides, nitro olefins, acid chlorides, enones, Et propiolate). The addition of (FG-R)₂Zn to aldehydes, in the presence of a chiral titanium catalyst derived from (1R,2R)-(-)-1,2-diaminocyclohexane (8 mol %), affords functionalized secondary alcs. in good yields (62-95%) and with very high enantiomeric excess (60-97%).

=> => d his 117-120

(FILE 'REGISTRY' ENTERED AT 17:39:10 ON 21 JUN 2004)

FILE 'HCAPLUS' ENTERED AT 17:40:35 ON 21 JUN 2004

L17 E KAPLAN G/AU,IN

348 S KAPLAN G?/AU,IN

E SIDDURI A/AU,IN

L18 18 S E5-E8

E TILLEY J/AU,IN

L19 102 S E3 OR E10 OR E16-E22

FILE 'HCAPLUS' ENTERED AT 17:46:22 ON 21 JUN 2004

L20 7 S (L17 AND L19) NOT L18

=>

=>

=> d ibib abs 120 1-7

L20 ANSWER 1 OF 7 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:872648 HCAPLUS

DOCUMENT NUMBER: 134:216797
 TITLE: Imide and lactam derivatives of N-benzylpyroglutamyl-L-phenylalanine as VCAM/VLA-4 antagonists
 AUTHOR(S): **Tilley, J. W.; Kaplan, G.;** Rowan, K.; Schwinge, V.; Wolitzky, B.
 CORPORATE SOURCE: Roche Research Center, Hoffmann-La Roche Inc., Nutley, NJ, 07110, USA
 SOURCE: Bioorganic & Medicinal Chemistry Letters (2000), Volume Date 2001, 11(1), 1-4
 CODEN: BMCLE8; ISSN: 0960-894X
 PUBLISHER: Elsevier Science Ltd.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB A series of imides and lactams derived from 4-amino-N-benzylpyroglutamyl-L-phenylalanine was prepared and evaluated for activity as VCAM/VLA-4 antagonists. Imides were more potent than the corresponding lactams; several had subnanomolar IC50s in an ELISA based assay and were also highly effective at blocking VLA-4 expressing Ramos cell binding to VCAM coated plates.
 REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 2 OF 7 HCAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 2000:419948 HCAPLUS
 DOCUMENT NUMBER: 133:171743
 TITLE: The design and synthesis of potent cyclic peptide VCAM-VLA-4 antagonists incorporating an achiral Asp-Pro mimetic
 AUTHOR(S): Fotouhi, Nader; Joshi, Pramod; Fry, David; Cook, Charles; **Tilley, Jefferson W.; Kaplan, Gerry;** Hanglow, Angela; Rowan, Karen; Schwinge, Virginia; Wolitzky, Barry
 CORPORATE SOURCE: Roche Research Center, Hoffmann-La Roche Inc, Nutley, NJ, 07110, USA
 SOURCE: Bioorganic & Medicinal Chemistry Letters (2000), 10(11), 1171-1173
 CODEN: BMCLE8; ISSN: 0960-894X
 PUBLISHER: Elsevier Science Ltd.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB The Asp-Pro sequence of the cyclic peptide Ac-HN-Tyr-Cys*-Asp-Pro-Cys*-OH could be replaced with the achiral dipeptide mimetic 1-(2-aminoethyl)cyclopentylcarboxylic acid with retention of potent inhibition of the VCAM-VLA-4 interaction.
 REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 3 OF 7 HCAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 2000:419946 HCAPLUS
 DOCUMENT NUMBER: 133:208152
 TITLE: Carbacyclic peptide mimetics as VCAM-VLA-4 antagonists
 AUTHOR(S): **Tilley, Jefferson; Kaplan, Gerry;** Fotouhi, Nader; Wolitzky, Barry; Rowan, Karen
 CORPORATE SOURCE: Roche Research Center, Hoffmann-La Roche Inc., Nutley, NJ, 07110, USA
 SOURCE: Bioorganic & Medicinal Chemistry Letters (2000), 10(11), 1163-1165
 CODEN: BMCLE8; ISSN: 0960-894X
 PUBLISHER: Elsevier Science Ltd.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 133:208152
 AB Substitution of C for S in a potent 13-membered cyclic disulfide-containing

peptide was accomplished via an intramol. Wittig reaction and resulted in a series of carba analogs. Potency in the VCAM/VLA-4 assay was sensitive to ring size and lower than that of the parent disulfide.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 4 OF 7 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:269113 HCAPLUS

DOCUMENT NUMBER: 133:17771

TITLE: N-Benzylpyroglutamyl-L-phenylalanine derivatives as VCAM/VLA-4 antagonists

AUTHOR(S): Chen, Li; **Tilley, Jefferson W.**; Guthrie, Robert W.; Mennona, Francis; Huang, Tai-Nan; **Kaplan, Gerry**; Trilles, Richard; Miklowski, Dorota; Huby, Nicolas; Schwinge, Virginia; Wolitzky, Barry; Rowan, Karen

CORPORATE SOURCE: Roche Research Center, Hoffmann-La Roche Inc., Nutley, NJ, 07110, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (2000), 10(8), 729-733
CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 133:17771

AB A series of 4-substituted N-(N-benzylpyroglutamyl)-L-phenylalanine derivs. was prepared as VLA-4/VCAM-1 antagonists. Analogs substituted by electron-deficient benzoylamino groups bearing bulky ortho substituents had low-nM potency in an ELISA assay and low-μM activity in a cell based assay.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 5 OF 7 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1997:483518 HCAPLUS

DOCUMENT NUMBER: 127:156432

TITLE: Identification of a Small Molecule Inhibitor of the IL-2/IL-2Rα Receptor Interaction Which Binds to IL-2

AUTHOR(S): **Tilley, Jefferson W.**; Chen, Li; Fry, David C.; Emerson, S. Donald; Powers, Gordon D.; Biondi, Denise; Varnell, Tracey; Trilles, Richard; Guthrie, Robert; Mennona, Francis; **Kaplan, Gerry**; LeMahieu, Ronald A.; Carson, Mathew; Han, Ru-Jen; Liu, C.-M.; Palermo, Robert; Ju, Grace

CORPORATE SOURCE: Roche Research Center, Hoffmann-La Roche Inc., Nutley, NJ, 07110, USA

SOURCE: Journal of the American Chemical Society (1997), 119(32), 7589-7590

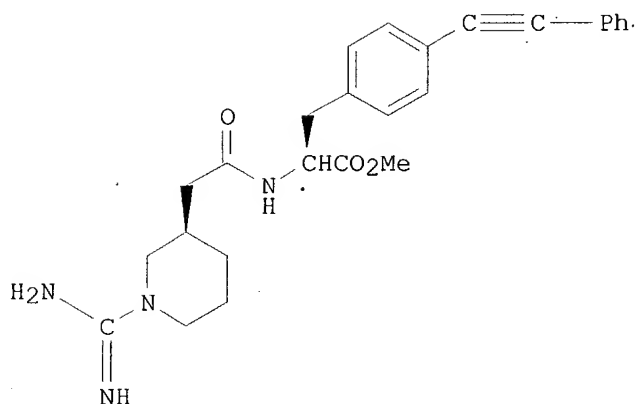
CODEN: JACSAT; ISSN: 0002-7863

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



AB In order to obtain small mols. capable of blocking interleukin-2 (IL-2)/IL-2 receptor α -chain (IL-2R α) interaction as orally based immunosuppressants, one member of a series of acylphenylalanine derivs. (I) was chosen; I inhibited IL-2/IL-2R α binding with an IC₅₀ of 3 μ M, whereas its enantiomer was inactive. The mechanism of the activity of I was studied using NMR. It appeared that I interferes with IL-2/IL-2R α binding by competing with IL-2R α for its binding site on IL-2.

L20 ANSWER 6 OF 7 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1991:23768 HCAPLUS

DOCUMENT NUMBER: 114:23768

TITLE: Propenyl carboxamide derivatives as antagonists of platelet-activating factor

AUTHOR(S): Guthrie, Robert W.; **Kaplan, Gerald L.**;
Mennona, Francis A.; **Tilley, Jefferson W.**;
Kierstead, Richard W.; O'Donnell, Margaret; Crowley,
Herman; Yaremko, Bohdan; Welton, Ann F.

CORPORATE SOURCE: Chem. Res. Dep., Hoffmann LaRoche Inc., Nutley, NJ,
07110, USA

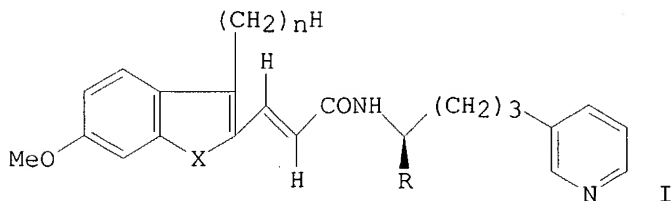
SOURCE: Journal of Medicinal Chemistry (1990), 33(10), 2856-64
CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 114:23768

GI



AB A series of N-[4-(3-pyridyl)butyl]-3-arylpropenamide derivs. was prepared and evaluated for platelet-activating factor (PAF) antagonist activity. These compds. represented conformationally constrained direct analogs of the corresponding potent 5-arylpentadieneamides. Most of the new compds. were active in a PAF-binding assay employing whole; washed dog platelets as the receptor source and inhibited PAF-induced bronchoconstriction in guinea pigs after i.v. administration. However, oral activity in the

PAF-induced bronchoconstriction model was highly sensitive to the nature and substitution of the bicyclic ring system. The most interesting compds. included naphthylpropenamides I ($X = \text{CH:CH}$, $n=4$, $R=\text{Me}$), benzothiophenylpropenamide I ($X = \text{S}$, $n = 5$, $R = \text{Me}$), and indolylpropenamide II ($X = \text{NMe}$, $n = 5$, $R = \text{Et}$), which inhibited PAF-induced bronchoconstriction in guinea pigs with ED50s of 3.0-5.4 mg/kg, when the animals were challenged 2 h after drug treatment. They were also highly effective 6 h after a 50 mg/kg oral dose. This study supports the notion that the key remote aromatic ring present in the 5-arylpentadieneamides is preferentially coplanar with the diene system for good PAF antagonist activity.

L20 ANSWER 7 OF 7 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1989:632526 HCAPLUS

DOCUMENT NUMBER: 111:232526

TITLE: Pentadienyl carboxamide derivatives as antagonists of platelet activating factor

AUTHOR(S): Guthrie, Robert W.; Kaplan, Gerald L.; Mennona, Francis A.; Tilley, Jefferson W.; Kierstead, Richard W.; Mullin, John G.; LeMahieu, Ronald A.; Zawoiski, Sonja; O'Donnell, Margaret; et al.

CORPORATE SOURCE: Roche Res. Cent., Hoffmann La Roche Inc., Nutley, NJ, 07110, USA

SOURCE: Journal of Medicinal Chemistry (1989), 32(8), 1820-35
CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 111:232526

AB A series of N-[4-(3-pyridinyl)butyl]-5,5-disubstituted-pentadienamides were prepared by acylation of appropriate amines with diphenylalkenoic acids and evaluated for platelet activating factor (PAF) antagonist activity. Compds. were assayed in vitro in a PAF-binding assay employing washed, whole dog platelets as the receptor source and in vivo after i.v. or oral administration for their ability to prevent PAF-induced bronchoconstriction in guinea pigs. Criteria required for good oral activity in the latter model include: an (E,E)-5-phenyl-2,4-pentadienamide, a second Ph or a four- or five-carbon alkyl moiety in the 5-position of the diene, and an (R)-[1-alkyl-4-(3-pyridinyl)butyl] substituent on the carboxamide nitrogen atom. The alkyl substituent on this side chain can be Me, Et, or cyclopropyl. Two members of this series, [R-(E)]-5,5-bis(4-methoxyphenyl)-N-[1-methyl-4-(3-pyridinyl)butyl]-2,4-pentadienamide (I) and [R-(E,E)]-5-(4-methoxyphenyl)-N-[1-methyl-4-(3-pyridinyl)butyl]-2,4-decadienamide (II) were selected for further pharmacol. evaluation. Both were found to be substantially longer acting after oral administration than the corresponding S enantiomers in the guinea pig bronchoconstriction assay. A second in vivo model used to evaluate PAF antagonists detcs. the ability of test compds. to decrease the area of skin wheals induced by an intradermal injection of PAF. In this model, using both rats and guinea pigs, compds. I and II were as active as the reference PAF antagonist 3-[4-(2-chlorophenyl)-9-methyl-6H-thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine-2-yl]-1-(4-morpholinyl)-1-propanone.

=> =>

=>

=> d his 117-122

(FILE 'REGISTRY' ENTERED AT 17:39:10 ON 21 JUN 2004)

FILE 'HCAPLUS' ENTERED AT 17:40:35 ON 21 JUN 2004

L17 E KAPLAN G/AU, IN
 348 S KAPLAN G?/AU, IN
 E SIDDURI A/AU, IN
 L18 18 S E5-E8
 E TILLEY J/AU, IN
 L19 102 S E3 OR E10 OR E16-E22

FILE 'HCAPLUS' ENTERED AT 17:46:22 ON 21 JUN 2004

L20 7 S (L17 AND L19) NOT L18
 L21 28 S (L17 OR L19) AND (PYRIDINYL? OR PHENYLALANINE?)
 L22 17 S L21 NOT (L18 OR L20)

=> d ibib abs 122 1-17

L22 ANSWER 1 OF 17 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:1463 HCAPLUS

DOCUMENT NUMBER: 136:325809

TITLE: N-Acyl-L-**phenylalanine** derivatives as potent VLA-4 antagonists that mimic a cyclic peptide conformation

AUTHOR(S): Chen, Li; **Tilley, Jefferson**; Trilles, Richard V.; Yun, Weiya; Fry, David; Cook, Charles; Rowan, Karen; Schwinge, Virginia; Campbell, Robert

CORPORATE SOURCE: Roche Research Center, Hoffmann-La Roche Inc., Nutley, NJ, 07110, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (2002), 12(2), 137-140

CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A series of N-benzylpyroglutamyl-L-**phenylalanine** derivs. bearing carbamoyl substituents in the 3- or 4-positions was prepared and assayed for inhibition of the interaction between VCAM and VLA-4. Potent inhibition was observed in a number of analogs with substitution in the 4-position favored over the 3-position. A crystal structure of the key intermediate N-(benzylpyroglutamyl)-3-(hydroxymethyl)-L-**phenylalanine** Me ester indicates that it accesses a low energy conformation which closely matches key pharmacophores of a structurally characterized cyclic peptide.

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 2 OF 17 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:269112 HCAPLUS

DOCUMENT NUMBER: 133:37726

TITLE: N-acyl **phenylalanine** analogues as potent small molecule VLA-4 antagonists

AUTHOR(S): Chen, Li; **Tilley, Jefferson W.**; Huang, Tai-Nan; Miklowski, Dorota; Trilles, Richard; Guthrie, Robert W.; Luk, Kin; Hanglow, Angela; Rowan, Karen; Schwinge, Virginia; Wolitzky, Barry

CORPORATE SOURCE: Roche Research Center, Hoffmann-La Roche, Inc., Nutley, NJ, 07110, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (2000), 10(8), 725-727

CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We have identified a series of low mol. weight (Mr <500) N-acylphenylalanines that are effective inhibitors of the VCAM-VLA-4 interaction. Investigation of the SAR of the N-acyl moiety led to the identification of N-benzylpyroglutamyl derivs. as being particularly potent.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 3 OF 17 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1995:277045 HCAPLUS

DOCUMENT NUMBER: 122:46487

TITLE: CAT-1 inhibitors, their synthesis, pharmaceutical compositions, and methods of use

INVENTOR(S): Guthrie, Robert W.; Mullin, John G., Jr.; Kachensky, David F.; Kierstead, Richard W.; **Tilley, Jefferson W.**; Heathers, Guy P.; Higgins, Alan J.; Lemahieu, Ronald A.

PATENT ASSIGNEE(S): Hoffman-La Roche Inc., USA

SOURCE: U.S., 85 pp. Cont.-in-part of U.S. Ser. No. 698, 014, abandoned.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

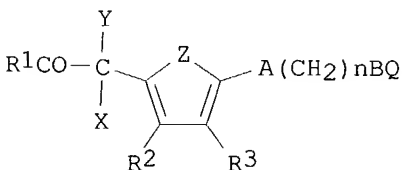
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5344843	A	19940906	US 1992-850620	19920313
RU 2059603	C1	19960510	RU 1992-5011784	19920131
EP 512352	A2	19921111	EP 1992-107135	19920427
EP 512352	A3	19930310		
EP 512352	B1	19960327		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, PT, SE				
AT 136018	E	19960415	AT 1992-107135	19920427
AU 9216003	A1	19921112	AU 1992-16003	19920504
AU 653398	B2	19940929		
CA 2068076	AA	19921110	CA 1992-2068076	19920506
ZA 9203279	A	19930127	ZA 1992-3279	19920506
NO 9201840	A	19921110	NO 1992-1840	19920508
HU 63602	A2	19930928	HU 1992-1538	19920508
JP 05279353	A2	19931026	JP 1992-143375	19920508
JP 07107060	B4	19951115		
RO 109938	B1	19950728	RO 1992-622	19920508
BR 9201769	A	19921229	BR 1992-1769	19920511

PRIORITY APPLN. INFO.:

US 1991-698014 B2 19910509
US 1992-850620 A 19920313

OTHER SOURCE(S): MARPAT 122:46487

GI



I

AB The invention relates to compds. I (R¹ = OH; R², R³ = H, alkyl, aryl, alkoxy, etc.; X, Y together = O, or one is amino and other is H; Z = S, CR²=CR^{2'}; A = bond, O, S, SO, CHCH, etc.; B = bond, O, S, SO, etc.; Q = Ph, cyclohexyl, **pyridinyl**, etc.; n = 1-6) and their pharmaceutically acceptable salts, and when appropriate, enantiomers, racemates, diastereomers or mixts. thereof or geometric isomer or mixts.

thereof, and pharmaceutically acceptable salts thereof. The compds. inhibit carnitine acyltransferase 1 (CAT-1) and are therefore useful in the prevention of injury to ischemic tissue, and can limit infarct size, improve cardiac function and prevent arrhythmias during and following a myocardial infarction. 5-[[2-(2-Naphthalenyloxy)ethyl]oxy]- α -oxo-2-thiopheneacetic acid (preparation given) inhibited CAT-1 with an IC₅₀ = 0.05 μ M. Tablet and capsule formulations containing 4-[2-(2-naphthyloxy)ethoxy]- α -oxobenzeneacetic acid are presented.

L22 ANSWER 4 OF 17 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1992:605355 HCAPLUS

DOCUMENT NUMBER: 117:205355

TITLE: Structure activity of C-terminal modified analogs of Ac-CCK-7

AUTHOR(S): **Tilley, Jefferson W.**; Danho, Waleed; Shiuey, Shian Jan; Kulesha, Irina; Sarabu, Ramakanth; Swistok, Joseph; Makofske, Raymond; Olson, Gary L.; Chiang, Elliot; et al.

CORPORATE SOURCE: Roche Res. Cent., Hoffmann LaRoche Inc., Nutley, NJ, USA

SOURCE: International Journal of Peptide & Protein Research (1992), 39(4), 322-36
CODEN: IJPPC3; ISSN: 0367-8377

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Previous work indicates that both the C-terminal **phenylalanine** amide and the tryptophan moieties of cholecystokinin (CCK) are critical pharmacophores for interaction with either the A or B receptor subtypes. The authors have examined a series of analogs of Ac-CCK-7 [Ac-Tyr(SO₃H)-Met-Gly-Trp-Met-Asp-Phe₃₃-NH₂] (I) in which the Ph ring of the C-terminal Phe-NH₂ has been modified. Compds. were assessed in binding assays using homogenated rat pancreatic membranes and bovine striatum as the source of CCK-A and CCK-B receptors resp. and for anorectic activity after i.p. administration to rats. Substitution of a number of cycloalkyl or bicyclic aryl moieties for the Ph ring of **phenylalanine₃₃** including cyclopentyl, cyclohexyl (II), cyclooctyl (III), 2-(5,6,7,8-tetrahydro)naphthyl (IV), 2-naphthyl (V), and 1-naphthyl (VI) led to analogs with 10-70 times the anorectic potency of I. The anorectic activity of II was blocked by the specific CCK-A receptor antagonist MK-329. Other bulky aliphatic groups in place of the **phenylalanine₃₃** aromatic ring such as iso-Pr, 2-adamantyl and cyclohexylmethyl gave derivs. similar to I in potency. While most of the new compds. were comparable to CCK in binding assays, III-VI were exceptionally potent with IC₅₀s 10-11-10-14 M in the pancreas. III and VI were further evaluated for their ability to stimulate amylase secretion and found to have potencies similar to that of CCK. The dissociation between potency in the binding and amylase secretion assays suggests that they may interact with a high affinity binding site which is not coupled to amylase secretion. Thus, CCK receptors possess a generous hydrophobic pocket capable of accommodating large alkyl groups in place of the side chain of **phenylalanine₃₃** and that the pharmacol. profile of CCK analogs can be tailored by appropriate exploitation of this finding.

L22 ANSWER 5 OF 17 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1991:123031 HCAPLUS

DOCUMENT NUMBER: 114:123031

TITLE: Carboxylic acids and tetrazoles as isosteric replacements for sulfate in cholecystokinin analogs

AUTHOR(S): **Tilley, Jefferson W.**; Danho, Waleed; Lovey, Kathleen; Wagner, Rolf; Swistok, Joseph; Makofske, Raymond; Michalewsky, Joseph; Triscari, Joseph; Nelson, David; Weatherford, Sally

CORPORATE SOURCE: Roche Res. Cent., Hoffmann-LaRoche Inc., Nutley, NJ,

07110, USA
 SOURCE: Journal of Medicinal Chemistry (1991), 34(3), 1125-36
 CODEN: JMCMAR; ISSN: 0022-2623
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 114:123031

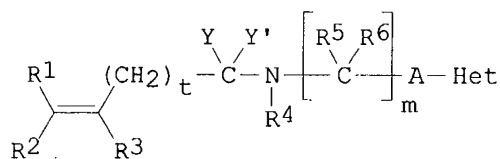
AB A series of analog of the satiety-inducing peptide cholecystokinin (CCK-8) was prepared in which the sulfated tyrosine required for activation of peripheral receptors was replaced with a carboxy(alkyl)- or tetrazolyl(alkyl)**phenylalanine** to investigate whether an organic acid could serve the role of the sulfate group at the receptor. The necessary intermediates were prepared by previously reported procedures or by alkylation of carboxy(alkyl)- or tetrazolyl(alkyl)-phenylmethyl bromides with a glycine-derived anion followed by protecting-group manipulations and these were incorporated into derivs. of acetyl-CCK-7 using solid-phase synthesis. Peptide analogs were evaluated in a CCK binding assay for affinity for either peripheral (CCK-A) receptors using homogenated rat pancreatic membranes as the receptor source or for central (CCK-B) receptors using bovine striatum as the receptor source. They were further evaluated for effects on food intake in rats after i.p. (i.p.) injection. A number of the compds. reported are active in the CCK-A receptor binding assay although less potent than acetyl-CCK-7 and decrease food intake with comparable potency to acetyl-CCK-7. In a meal feeding model designed to assess appetite suppressant activity, acetyl CCK-7 has an ED50 of 7 nmol/kg i.p., while the ED50 values of peptides Ac-L-NHCH(CH₂C₆H₄R-4)CO-Met-Gly-Trp-Met-Asp-Phe-NH₂ (R = CH₂CO₂H, 2H-tetrazol-5-yl) were 9 and 11 nmol/kg, i.p., resp.

L22 ANSWER 6 OF 17 HCAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 1991:82465 HCAPLUS
 DOCUMENT NUMBER: 114:82465
 TITLE: Preparation of carboalkoxyalkylphenylalanine derivatives from tyrosine
 AUTHOR(S): **Tilley, Jefferson W.**; Sarabu, Ramakanth; Wagner, Rolf; Mulkerins, Kathleen
 CORPORATE SOURCE: Roche Res. Cent., Hoffmann LaRoche Inc., Nutley, NJ, 07110, USA
 SOURCE: Pept.: Chem., Struct. Biol., Proc. Am. Pept. Symp., 11th (1990), Meeting Date 1989, 939-40. Editor(s): Rivier, Jean E.; Marshall, Garland R. ESCOM Sci. Pub.: Leiden, Neth.
 CODEN: 56XTA7
 DOCUMENT TYPE: Conference
 LANGUAGE: English

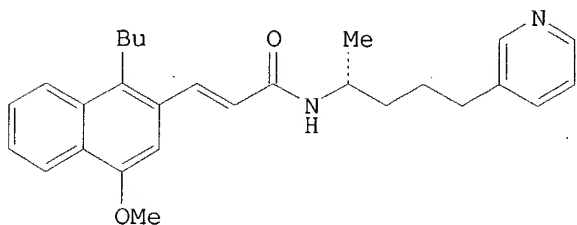
AB A symposium report on the preparation of the title **phenylalanine** derivs. from tyrosine.

L22 ANSWER 7 OF 17 HCAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 1990:631218 HCAPLUS
 DOCUMENT NUMBER: 113:231218
 TITLE: Preparation of heterocyclic (especially pyridine) compounds useful in treating diseases characterized by excess platelet activating factor (PAF)
 INVENTOR(S): Guthrie, Robert W.; Kierstead, Richard W.; Mullin, John G.; **Tilley, Jefferson W.**
 PATENT ASSIGNEE(S): Hoffmann-La Roche, Inc., USA
 SOURCE: U.S., 50 pp. Cont.-in-part of U.S. Ser. No. 179,616, abandoned.
 CODEN: USXXAM
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4927838	A	19900522	US 1988-215464	19880705
ZA 8804859	A	19890426	ZA 1988-4859	19880706
IL 87019	A1	19930708	IL 1988-87019	19880706
DK 8803780	A	19890111	DK 1988-3780	19880707
AU 8818825	A1	19890112	AU 1988-18825	19880707
AU 611460	B2	19910613		
FI 8803289	A	19890111	FI 1988-3289	19880708
NO 8803082	A	19890111	NO 1988-3082	19880708
HU 47909	A2	19890428	HU 1988-3583	19880708
HU 203873	B	19911028		
JP 01085963	A2	19890330	JP 1988-171719	19880710
PRIORITY APPLN. INFO.:			US 1987-72199	19870710
			US 1988-179616	19880411
OTHER SOURCE(S):		MARPAT 113:231218		
GI				



I



II

AB Title compds. I [Y = Y' = H; or YY' = O, S; A = p-C₆H₄ or (CH₂)_nXs(CH₂)_r; X = O, S, CH:CH, n, r = 0-3; m, s = 0-1; (n + m) ≥ 2 when s = 1; t = 0-10; R₁, R₂ = alkyl, alkenyl, aryl; or 1 of R₁ and R₂ = H and the other is substituted (dihydro)naphthyl, indenyl, benzofuryl, benzothienyl, indolyl; R₃ = H, alkyl, aryl; R₄ = H, alkyl, aryl, acyl; R₅ = H, alkyl; R₆ = H, alkyl, cycloalkyl, heterocyclyalkyl, aryl; Met = (substituted) 6-membered heteroaryl containing 1-2 N atoms] were prepared. For example, 1-butyl-4-methoxy-2-naphthalenecarboxaldehyde underwent Wittig reaction with Ph₃P:CHCO₂Me, followed by hydrolysis, reesterification with 4-nitrophenol, and amidation with (R)-α-methyl-3-pyridinebutanamine, to give (naphthalenyl)(pyridinylbutyl)propenamine derivative II. At 1 mg/kg i.v. in anesthetized guinea pig, II gave 90% inhibition of PAF-induced bronchoconstriction. Seven formulations, preps. of approx. 30 I and over 150 precursors, and addnl. biol. data are given.

L22 ANSWER 8 OF 17 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1990:478171 HCAPLUS

DOCUMENT NUMBER: 113:78171

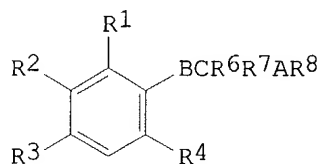
TITLE: Substituted N-[(pyridyl)alkyl]arylcarboxamides as platelet activating factor antagonists

INVENTOR(S): Tilley, Jefferson W.; Guthrie, Robert W.; Clader, John W.; LeMahieu, Ronald A.

PATENT ASSIGNEE(S): Hoffmann-La Roche, Inc., USA

SOURCE: U.S., 40 pp.
 CODEN: USXXAM
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4916145	A	19900410	US 1987-72386	19870710
PRIORITY APPLN. INFO.:			US 1987-72386	19870710
OTHER SOURCE(S):		CASREACT 113:78171; MARPAT 113:78171		
GI				

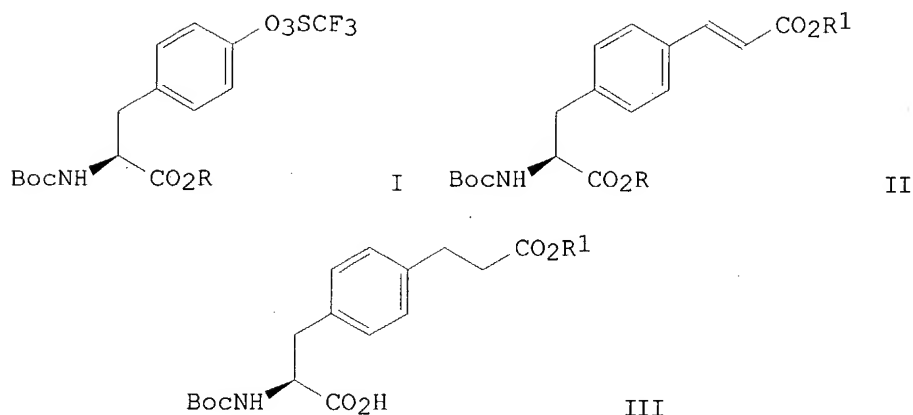


I

AB The title compds. [I; R1, R4 = H, halo, alkyl, OH, alkoxy; R2, R3 = H, alkyl, cycloalkyl, halo, NO2, alkoxy, alkenyl, alkynyl, (substituted) Ph, naphthalenyl; R5, R6 = H, alkyl; R7 = H, alkyl, cycloalkyl, (substituted) Ph, naphthalenyl; B = C(Y)NR5, tetrazolylene; Y = O, S; A = (CH2)n Xm(CH2)r; n, r = 0-3; m = 0, 1; R8 = (bicyclic) heteroaryl, e.g., (substituted) pyridyl], were prepared. Thus, biphenyl-4-carboxylic acid in CH2Cl2 was refluxed with SOCl2 and DMF. 3-Pyridinebutanamine was added to the cooled mixture to give N-[4-(3-pyridinyl)butyl]-(1,1'-biphenyl)-4-carboxamide. I at 50 mg/kg orally inhibited PAF-induced bronchoconstriction in guinea pigs by 33-93%. Oral dosage forms were prepared containing R-3',4'-dimethoxy-N-[1-methyl-4-(3-pyridinyl)butyl]-(1,1'-biphenyl)-4-carboxamide.

L22 ANSWER 9 OF 17 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1990:77898 HCAPLUS
 DOCUMENT NUMBER: 112:77898
 TITLE: Preparation of carboalkoxyalkylphenylalanine derivatives from tyrosine
 AUTHOR(S): Tilley, Jefferson W.; Sarabu, Ramakanth; Wagner, Rolf; Mulkerins, Kathleen
 CORPORATE SOURCE: Roche Res. Cent., Hoffmann La Roche, Inc., Nutley, NJ, 07110, USA
 SOURCE: Journal of Organic Chemistry (1990), 55(3), 906-10
 CODEN: JOCEAH; ISSN: 0022-3263
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 112:77898
 GI



AB In order to provide the means for the synthesis of peptides incorporating stable and relatively nonpolar mimics of tyrosine phosphates and sulfates, procedures have been developed for the conversion of tyrosine derivs. to carbalkoxyalkylphenylalanines. Thus, tyrosine triflates I (Boc = Me₃CO₂C; R = CHPh₂, CH₂Ph) are coupled with an acrylate ester or preferably a 2-(trialkylstannyl)acrylate in the presence of Pd(PPh₃)₂Cl₂ to give carbalkoxyethenylphenylalanine derivs. II (R = CHPh₂, R¹ = CMe₃; R = CH₂Ph, R¹ = Me). Hydrogenation of II affords the carbalkoxyethylphenylalanine derivs. III (R¹ = same). For the preparation of carbalkoxymethylphenylalanines I (R = CH₂Ph, Me) are coupled with CH₂=CHCH₂SnBu₃ in the presence of Pd(PPh₃)₂Cl₂ and LiCl to give an ester of 4-allylphenylalanine. A two-stage oxidation using RuO₄-NaIO₄ followed by NaO₂Cl in phosphate buffer gives a carboxymethylphenylalanine. Esterification of the newly formed carboxylic acid and selective deesterification of the α-carboxylate completes the synthesis.

L22 ANSWER 10 OF 17 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1989:614392 HCAPLUS

DOCUMENT NUMBER: 111:214392

TITLE: Preparation of pyridine-containing cyclopropylpropenamides as platelet activating factor (PAF) antagonists

INVENTOR(S): Guthrie, Robert W.; Kierstead, Richard W.;
Tilley, Jefferson W.

PATENT ASSIGNEE(S): Hoffmann-La Roche, Inc., USA

SOURCE: U.S., 44 pp.

CODEN: USXXAM

DOCUMENT TYPE: Patent

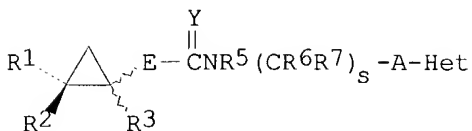
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4786646	A	19881122	US 1987-72390	19870710
US 4927826	A	19900522	US 1988-238224	19880830
PRIORITY APPLN. INFO.:			US 1987-72390	19870710
OTHER SOURCE(S):		CASREACT 111:214392; MARPAT 111:214392		

GI



AB The title compds. [I; Y = O, S; A = p-phenylene, (CH₂)_nX_m(CH₂)_r; X = O, S, CH:CH; n, r = 0-3; s, m = 0, 1; m; provided that n + s must be at least 2; R₁, R₂ = H, lower alkyl, cycloalkyl, lower alkenyl, naphthalenyl, Ph, Ph or naphthalenyl mono- or disubstituted by halo, CF₃, lower alkyl, Ph, lower alkoxy, or NO₂; E = CR₄:CR₈, (CH₂)_k; k = 0-4; R₃-R₆, R₈ = H, lower alkyl; R₇ = H, lower alkyl, cycloalkyl, **pyridinyl**-lower alkyl, Ph or naphthalenyl optionally mono- or disubstituted by halo, CF₃, lower alkyl, Ph, lower alkoxy, or NO₂; Het = (substituted) pyridyl], or enantiomers, diastereomers, or racemic mixts. thereof, exhibiting activity as platelet activating factor (PAF) antagonists and useful as drugs, were prepared [1(R,S),2(R,S)-(E)]-2-[[2-(3-Methoxyphenyl)-2-phenyl]cyclopropyl]-2-propenoic acid 4-nitrophenyl ester (preparation given) (1.6 g) was treated with 0.64 g 3-pyridinebutanamine in THF at ambient temperature for 2 h to give [1(R,S),2(R,S)-(E)]-3-[[2-(3-methoxyphenyl)-2-phenyl]cyclopropyl]-N-[4-(3-**pyridinyl**)butyl]-2-propenamide (II). II inhibited the binding of PAF to dog platelets in vitro with an IC₅₀ of 8 nM. An inhalation aerosol formulation comprising [S-(E)]-3-[2,2-bis(4-fluorophenyl)cyclopropyl]-N-[4-(3-**pyridinyl**)butyl]-2-propenamide (III) 1.0, sorbitan trioleate 0.5, Freon 12 64.0, Freon 11 18.5, and Freon 114 16.0 weight % was prepared

L22 ANSWER 11 OF 17 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1989:573987 HCAPLUS

DOCUMENT NUMBER: 111:173987

TITLE: Heterocyclic alkenamides and derivatives, particularly (**pyridinylalkyl**)alkenamides, useful as antagonists of platelet activating factor, and their preparation, compositions, and use

INVENTOR(S): Guthrie, Robert William; Kierstead, Richard Wightman; Mullin, John Guilfoyle, Jr.; **Tilley, Jefferson Wright**

PATENT ASSIGNEE(S): Hoffmann-La Roche, F., und Co. A.-G., Switz.

SOURCE: Eur. Pat. Appl., 72 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 298466	A2	19890111	EP 1988-110814	19880706
EP 298466	A3	19901024		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
ZA 8804859	A	19890426	ZA 1988-4859	19880706
IL 87019	A1	19930708	IL 1988-87019	19880706
DK 8803780	A	19890111	DK 1988-3780	19880707
AU 8818825	A1	19890112	AU 1988-18825	19880707
AU 611460	B2	19910613		
FI 8803289	A	19890111	FI 1988-3289	19880708
NO 8803082	A	19890111	NO 1988-3082	19880708
HU 47909	A2	19890428	HU 1988-3583	19880708
HU 203873	B	19911028		
JP 01085963	A2	19890330	JP 1988-171719	19880710

PRIORITY APPLN. INFO.:

US 1987-72199 19870710

US 1988-179616

19880411

OTHER SOURCE(S): MARPAT 111:173987

AB Title compds. R1R2C:CR3(CH2)tCY1NR4(CR5R6)mAR [I; Y = Y' = H, or YY' = O, S; A = p-C6H4, (CH2)n(X)s(CH2)r; X = O, S, CH:CH; n, r = 1; t = 0-10; R1, R2 = alkyl, alkenyl, aryl; or 1 of R1 and R2 = H and other = aryl group Q; W = CX3:CX4, CH2CH2, CH2, O, S, NX5; X1 = alkyl, (un)substituted Ph; X2-X4 = H, alkyl, alkoxy, halo; X5 = alkyl; R3 = H, alkyl, aryl; R4 = H, alkyl, aralkyl, aryl, acyl; R5 = H, alkyl; R6 = H, alkyl, cycloalkyl, aryl, heterocyclalkyl; R = (un)substituted 6-membered heteroaryl with 1-2 N atoms] are prepared as antagonists of platelet activating factor (PAF). 6-Methoxytetralone was converted in 5 steps to (E)-3-(1-butyl-6-methoxy-2-naphthalenyl)-2-propenoic acid (II) Me ester. Saponification by NaOH in aqueous MeOH gave II, which was reesterified using DCC and 4-nitrophenol to give II 4-nitrophenyl ester. Direct amidation of the latter with (R)- α -methyl-3-pyridinebutanamine in THF gave N-(pyridylbutyl)naphthylpropenamide III. At 1 mg/kg i.v. in anesthetized guinea pigs, III gave 95% inhibition of PAF-induced bronchoconstriction. An aerosol solution contained III 1.0, EtOH 30.0, ascorbic acid 0.5, Freon 12 54.8, and Freon 114 13.7 weight %.

L22 ANSWER 12 OF 17 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1989:533959 HCAPLUS

DOCUMENT NUMBER: 111:133959

TITLE: Biphenylcarboxamide derivatives as antagonists of platelet-activating factor

AUTHOR(S): **Tilley, Jefferson W.**; Clader, John W.; Zawoiski, Sonja; Wirkus, Maria; LeMahieu, Ronald A.; O'Donnell, Margaret; Crowley, Herman; Welton, Ann F.
CORPORATE SOURCE: Roche Res. Cent., Hoffmann La Roche Inc., Nutley, NJ, 07110, USA

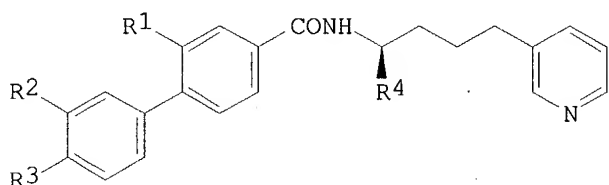
SOURCE: Journal of Medicinal Chemistry (1989), 32(8), 1814-20
CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 111:133959

GI



AB A series of N-[4-(3-pyridinyl)butyl]-1,1'-biphenyl-4-carboxamides I (R1 = H, F, Ph, 3-MeOC6H4, 4-MeOC6H4, NO2, Br, MeO, HC.tplbond.C, Et, allyl, Pr, Bu, R2 = H, F, Me, OMe; R3 = H, OMe; R4 = H, Me) was prepared, and the compds. were evaluated for platelet-activating factor (PAF) antagonist activity in a binding assay employing washed, whole dog platelets and in vivo for their ability to inhibit PAF-induced bronchoconstriction in the guinea pig. The inclusion of a Me group in the R configuration on the side-chain carbon adjacent to the carboxamide nitrogen atom of these derivs. resulted in a marked enhancement of potency in the binding assay for compds. unsubstituted in the biphenyl 2-position and, more importantly, in improved oral bioavailability. Previous work with related pyrido[2,1-b]quinazoline-8-carboxamides suggests that the presence of such an alkyl group improves bioavailability by rendering the resulting compds. resistant to degradation by liver amidases. The most interesting compds. to emerge from this work are (R)-I (R1 = Br, Bu, R2 =

R3 = OMe, R4 = Me), each of which inhibits PAF-induced bronchoconstriction in the guinea pig by >55%, 6 h after an oral dose of 50 mg/kg.

L22 ANSWER 13 OF 17 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1989:212619 HCAPLUS

DOCUMENT NUMBER: 110:212619

TITLE: Preparation and formulation of diaryl-N-(**pyridinylalkyl**)pentadieneamides as platelet activating factor (PAF) antagonists

INVENTOR(S): Guthrie, Robert W.; Kierstead, Richard W.;
Tilley, Jefferson W.

PATENT ASSIGNEE(S): Hoffmann-La Roche, Inc., USA

SOURCE: U.S., 69 pp.
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

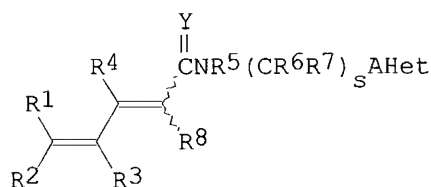
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4788206	A	19881129	US 1987-72389	19870710
ZA 8804857	A	19890426	ZA 1988-4857	19880706
DK 8803781	A	19890111	DK 1988-3781	19880707
FI 8803290	A	19890111	FI 1988-3290	19880708
NO 8803084	A	19890111	NO 1988-3084	19880708
AU 8818851	A1	19890112	AU 1988-18851	19880708
AU 626526	B2	19920806		
EP 299379	A1	19890118	EP 1988-110934	19880708
EP 299379	B1	19930421		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
HU 48594	A2	19890628	HU 1987-3584	19880708
HU 205902	B	19920728	HU 1988-3584	19880708
AT 88466	E	19930515	AT 1988-110934	19880708
ES 2054740	T3	19940816	ES 1988-110934	19880708
JP 01031766	A2	19890202	JP 1988-171720	19880710
US 4975438	A	19901204	US 1988-241174	19880906

PRIORITY APPLN. INFO.: US 1987-72389 19870710
EP 1988-110934 19880708

OTHER SOURCE(S): CASREACT 110:212619; MARPAT 110:212619

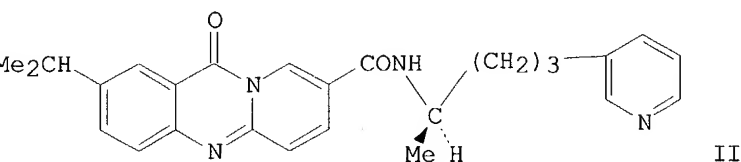
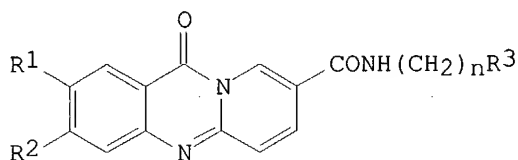
GI



AB The title compds. [I; R1, R1 = H, alkyl, cycloalkyl, alkenyl, **pyridinyl**, (un)substituted Ph, naphthalenyl; R3, R4, R8 = H, alkyl, (un)substituted Ph, naphthalenyl; R5, R6 = H, alkyl; R7 = H, alkyl, cycloalkyl, **pyridinylalkyl**, (un)substituted Ph, naphthalenyl; Y = O, S; A = p-phenylene, (CH2)nXm(CH2)r; X = O, S, CH:CH; n, r = 0-3; s = 0, 1; m = 0, 1; Het = (un)substituted **pyridinyl**], their enantiomers, racemates, geometrical isomers, and their pharmaceutically acceptable salts, were prepared 5,5-Bis(2-methoxyphenyl)-2,4-pentadienoic acid and 4-O2NC6H4OH in CH2Cl2 were treated with dicyclohexylcarbodiimide to give the ester which was condensed with 2-pyridinebutanamine in THF to

give (E)-I [A = (CH₂)₃, R₁ = R₂ = 2-MeOC₆H₄, R₃-R₈ = H, Y = O, Het = 3-pyridinyl, s = 1,] (II). II inhibited PAF with an IC₅₀ of 2 mM. An inhalation aerosol formulation comprised [R-(E,E)]-I [R₁ = Me(CH₂)₃, R₂ = 4-MeOC₆H₄, Y = O, R₄-R₆ = R₈ = H, R₇ = Me, A = (CH₂)₃, Het = 3-pyridinyl] 1, EtOH 30, ascorbic acid 0.5, Freon 12 54.8, and Freon 114 13.7 weight%.

22 ANSWER 14 OF 17 HCAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 1988:75343 HCAPLUS
 DOCUMENT NUMBER: 108:75343
 TITLE: Pyrido[2,1-b]quinazolinecarboxamide derivatives as platelet activating factor antagonists
 AUTHOR(S): Tilley, Jefferson W.; Burghardt, Barbara; Burghardt, Charles; Mowles, Thomas F.; Leinweber, Franz Josef; Klevans, Larry; Young, Richard; Hirkaler, Gerry; Fahrenholtz, Kenneth; et al.
 CORPORATE SOURCE: Chem. Res. Dep., Hoffmann-La Roche Inc., Nutley, NJ, 07110, USA
 SOURCE: Journal of Medicinal Chemistry (1988), 31(2), 466-72
 CODEN: JMCMAR; ISSN: 0022-2623
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 108:75343
 GI



AB A series of N-[(heteroaryl)alkyl]pyrido[2,1-b]quinazolines, e.g. I (R₁ = Me₂CH; R₂ = H; n = 2-7; R₃ = **pyridinyl**, pyrimidinyl, etc.) were prepared and evaluated for their ability to inhibit the binding of radiolabeled platelet activating factor (PAF) to its receptor on dog platelets. The most potent compds. in this series were pyrido[2,1-b]quinazoline-8-carboxamides possessing a four or six-carbon chain between the carboxamide N atom and a 3-**pyridinyl** or 5-pyrimidinyl moiety. Since earlier metabolism studies with pyridoquinazolinecarboxamides suggest that the carboxamide moiety is labile to hydrolysis in vivo, attempts were made to find isosteric replacements for this group. The substitutions examined led to a loss of activity; however, insertion of a Me group on the C atom α to the carboxamide N led to an enantioselective enhancement of potency. (R)-Oxopyridoquinazolinecarboxamide II was more potent than the corresponding S enantiomer in the PAF binding assay and was also shown to be more resistant to degradation by amidases present in whole liver homogenates obtained from guinea pig, dog, and squirrel monkey. The corresponding racemic compound (III) was found to inhibit transient PAF-induced thrombocytopenia and decreases in blood pressure in guinea

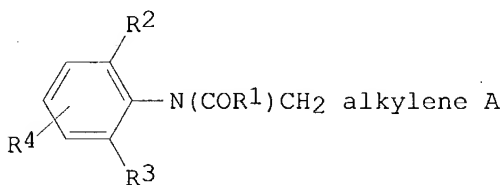
pigs after i.v. or oral administration and to have a duration of action of >5 h after an oral dose of 200 mg/kg. Compound III thus represents the prototype of a new class of orally active PAF antagonists.

L22 ANSWER 15 OF 17 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1987:32533 HCAPLUS
 DOCUMENT NUMBER: 106:32533
 TITLE: Substituted aniline derivatives
 INVENTOR(S): Mullin, John Guilfoyle, Jr.; Nakamura, Keiji;
Tilley, Jefferson Wright; Watanabe, Hiroshi
 PATENT ASSIGNEE(S): Hoffmann-La Roche, F., und Co. A.-G., Switz.
 SOURCE: Eur. Pat. Appl., 41 pp.
 CODEN: EPXXDW
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 198325	A2	19861022	EP 1986-104488	19860402
EP 198325	A3	19871007		
EP 198325	B1	19920715		
R: AT, BE, CH, DE, FR, GB, IT, LI, NL				
US 4696930	A	19870929	US 1985-722650	19850412
AT 78248	E	19920815	AT 1986-104488	19860402
JP 61251664	A2	19861108	JP 1986-83269	19860412
JP 06099393	B4	19941207		
US 4891429	A	19900102	US 1987-62028	19870615
PRIORITY APPLN. INFO.:			US 1985-722650	19850412
			EP 1986-104488	19860402

OTHER SOURCE(S): CASREACT 106:32533
 GI

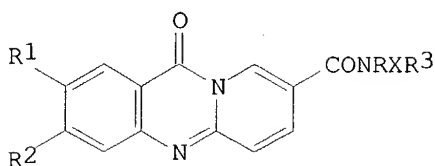


AB Title compds. I [R1 = alkylene-NH2, alkylene-A; alkylene = C1-5 alkylene; A = (un)substituted **pyridinyl**, imidazolyl, pyrimidinyl; R2, R3, R4 = H, Me] and their salts, useful as thromboxane synthase inhibitors, platelet aggregation inhibitors, and antiarrhythmics, were prepared. Thus, 2,6-dimethylaniline was reacted with 3-pyridylpropyl bromide-HBr to give N-(2,6-dimethylphenyl)-3-pyridylpropanamine which was treated with 2,3-dihydro-1,3-dioxo-1H-isoin-dole- α -methylacetyl chloride to give the appropriate isoindoleacetamide which in DMF was reacted with MeNH2 to give (\pm)-2-amino-N-(2,6-dimethylphenyl)-N-[3-(3-pyridyl)propyl]propanamide (II). II as the di-HCl salt at 4.4 mg/kg i.v., was effective against ouabain-induced arrhythmia in dogs and at 50 mg/kg orally, inhibited rabbit platelet aggregation. A tablet formulation contained II \cdot 2HCl 100, 250, and 500 mg/tablet.

L22 ANSWER 16 OF 17 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1987:12535 HCAPLUS

DOCUMENT NUMBER: 106:12535
 TITLE: N-(heterocyclic alkyl)pyrido[2,1-b]quinazoline-8-carboxamides as orally active antiallergy agents
 AUTHOR(S): **Tilley, Jefferson W.**; Levitan, Paul; Lind, Joan; Welton, Ann F.; Crowley, Herman J.; Tobias, Lawrence D.; O'Donnell, Margaret
 CORPORATE SOURCE: Chem. Res. Dep., Hoffmann-La Roche, Inc., Nutley, NJ, 07110, USA
 SOURCE: Journal of Medicinal Chemistry (1987), 30(1), 185-93
 CODEN: JMCMAR; ISSN: 0022-2623
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 106:12535
 GI



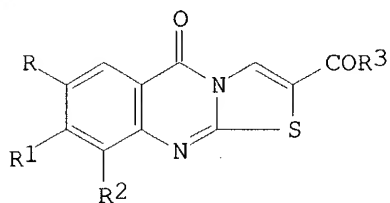
AB A series of 27 title compds. [I, R = H or Me; R1 = H, Me, MeO, iso-Pr, Me2CHO, OH, or Br; R2 = H, Me, MeO, or Cl or R1R2 = (CH2)4; R3 = 2-, 3-, or 4-pyridinyl, 3-pyrimidinyl, imidazolyl, or 2-methylimidazolyl; X = (CH2)n, (CH2)40, CH2CH2SCH2, etc.; n = 2-7] were prepared, mostly by coupling of the appropriate amine with pyridoquinazolinecarboxylic acids, either through the acid chlorides or using diphenylphosphoryl azide, and tested for their ability to antagonize slow-reacting substance of anaphylaxis-induced contraction of guinea pig ileum and to inhibit thromboxane synthase [61276-89-9] in vitro. I bearing a branched-chain alkyl moiety in the 2-position and a C4-6 linear chain between a 3- or 4-substituted pyridine or a 1-substituted imidazole ring and the carboxamide N showed the best combination of potency in the 2 assays. One of the most potent analogs, 2-(1-methylethyl)-N-[4-(1H-imidazol-1-yl)butyl]-11-oxo-11H-pyrido[2,1-b]quinazoline-8-carboxamide (II) [88939-84-8] was not a specific inhibitor of LTE4-induced symptomol. in vivo, but exhibited a more general activity by inhibiting bronchospasm in guinea pigs induced by LTC4, LTD4, platelet-activating factor (PAF), and histamine and skin-wheal formation in rats and guinea pigs induced by LTC4, LTD4, and PAF. In addition, II was orally active in the passive cutaneous anaphylaxis assay, suggesting that it also exhibits mediator release-inhibitory activity. Thus, I may be useful for the treatment of asthma.

L22 ANSWER 17 OF 17 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1985:560530 HCAPLUS
 DOCUMENT NUMBER: 103:160530
 TITLE: Thiazoloquinazoline derivatives and their therapeutic use
 INVENTOR(S): Carson, Matthew; Lemahieu, Ronald Andrew; **Tilley, Jefferson Wright**
 PATENT ASSIGNEE(S): Hoffmann-La Roche, F., und Co. A.-G., Switz.
 SOURCE: Eur. Pat. Appl., 43 pp.
 CODEN: EPXXDW
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 142057	A2	19850522	EP 1984-112495	19841017
EP 142057	A3	19880330		
R: CH, DE, FR, GB, IT, LI				
JP 60112794	A2	19850619	JP 1984-230466	19841102
PRIORITY APPLN. INFO.:			US 1983-548758	19831104

GI



AB Thiazoloquinazolinonecarboxylic acid esters and amides I [R = H, alkyl, cycloalkyl, alkoxy, OH, halo, alkylthio, alkylsulfinyl, alkylsulfonyl, dialkylaminoalkoxy, 2-hydroxyethoxy; R1 = H, alkyl; R2 = H, alkyl, alkoxy; R3 = (un)substituted alkylamino, aminoalkylamino, aminoalkoxy] were prepared. Thus, 2-amino-5-(1-methylethyl)benzoic acid was treated with 5-carbomethoxy-2-chlorothiazole and HCO₂H to give I (R = CHMe₂, R1, R2 = H, R3 = OMe) which was hydrolyzed, then treated with SOCl₂ and 3-pyridine butanamine to give I [R = CHMe₂, R1, R2 = H, R3 = 4-(3-pyridyl)butylamino] (II). In guinea pigs at 10 mg/kg i.v. II gave a 68% inhibition of leukotriene E₄-induced bronchoconstriction.

=>

=> fil hcaplus

FILE 'HCAPLUS' ENTERED AT 18:07:52 ON 21 JUN 2004

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

Copyright of the articles to which records in this database refer is held by the publishers listed in the PUBLISHER (PB) field (available for records published or updated in Chemical Abstracts after December 26, 1996), unless otherwise indicated in the original publications. The CA Lexicon is the copyrighted intellectual property of the the American Chemical Society and is provided to assist you in searching databases on STN. Any dissemination, distribution, copying, or storing of this information, without the prior written consent of CAS, is strictly prohibited.

FILE COVERS 1907 - 21 Jun 2004 VOL 140 ISS 26

FILE LAST UPDATED: 20 Jun 2004 (20040620/ED)

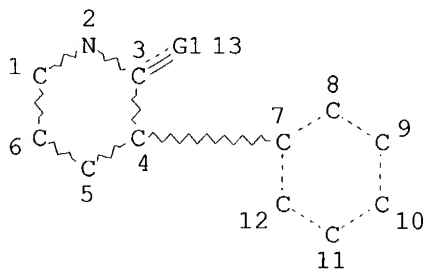
This file contains CAS Registry Numbers for easy and accurate substance identification.

=>

=>

=> d stat que 128

L23 STR



VAR G1=O/S

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

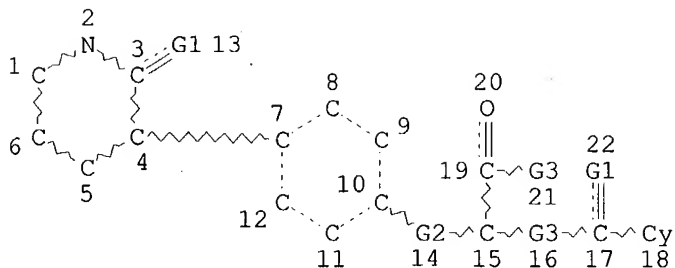
RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 13

STEREO ATTRIBUTES: NONE

L25 9271 SEA FILE=REGISTRY SSS FUL L23

L26 STR



VAR G1=O/S
 REP G2=(1-2) C
 VAR G3=O/N
 NODE ATTRIBUTES:
 DEFAULT MLEVEL IS ATOM
 DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
 RING(S) ARE ISOLATED OR EMBEDDED
 NUMBER OF NODES IS 22

STEREO ATTRIBUTES: NONE

L27 104 SEA FILE=REGISTRY SUB=L25 SSS FUL L26
 L28 3 SEA FILE=HCAPLUS ABB=ON PLU=ON L27

=>
 =>

=> d ibib abs hitrn l28 1-3

L28 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:511294 HCAPLUS

DOCUMENT NUMBER: 139:85646

TITLE: Preparation of novel phenylalanine derivatives as
 α 4 integrin inhibitors

INVENTOR(S): Okuzumi, Tatsuya; Sagi, Kazuyuki; Yoshimura,
 Toshihiko; Tanaka, Yuji; Nakanishi, Eiji; Ono, Miho;
 Murata, Masahiro

PATENT ASSIGNEE(S): Ajinomoto Co., Inc., Japan

SOURCE: PCT Int. Appl., 124 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003053926	A1	20030703	WO 2002-JP13070	20021213
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,			

MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:

JP 2001-380655 A 20011213

JP 2002-39070 A 20020215

OTHER SOURCE(S):

MARPAT 139:85646

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Phenylalanine derivs. represented by the following formula (I), their analogs, and pharmaceutically acceptable salts thereof [wherein A = Q-Q5; Arm = cycloalkyl or aromatic ring containing 0-4 heteroatoms selected from O, S, and N; R1 = H, (un)substituted alkyl, cycloalkyl-lower alkyl or cycloalkyl optionally containing a heteroatom in the ring, aryl-lower alkyl, heteroaryl-lower alkyl, lower hydroxyalkyl, lower haloalkyl, (un)substituted alkenyl, lower haloalkyl, (un)substituted alkynyl, aryl, heteroaryl, lower alkoxy, carbonyl, (un)substituted CONH2, lower alkanoyl, aroyl, lower alkylsulfonyl, (un)substituted SO2NH2; R2-R6, R10-R33 = groups listed in R1, halo, OH, lower alkoxy, lower alkylthio, cycloalkyl-lower alkyl or -alkylthio optionally containing a heteroatom in the ring, (hetero)aryl-lower alkoxy or -lower alkylthio, lower hydroxyalkoxy, lower haloalkoxy, etc.; B = HO, alkoxy, (un)substituted lower alkoxy, hydroxyamino; when A = Q, Q1, Q2, Q3, or Q4, C = aryl, heteroaryl, cycloalkyl or cycloalkyl-lower alkyl optionally containing a heteroatom in the ring, (hetero)aryl-lower alkyl, (un)substituted alkyl, etc.; when A = Q5, C = C(D) (D1)COE (wherein D, D1 = H, each (un)substituted lower alkyl, lower alkenyl, or alkynyl; E = amino, (un)substituted alkylamino, etc.); J, J1 = H, halo, lower alkyl, lower alkoxy, NO2, NH2, HO] are prepared. These show an $\alpha 4$ integrin inhibitory activity and are usable as remedies or preventives for various diseases, for example, in which the $\alpha 4$ integrin-dependent adhesion process relating to $\alpha 4$ integrin participates in pathol. conditions, such as inflammatory diseases, rheumatoid arthritis, inflammatory bowel disease, systemic lupus erythematosus, multiple sclerosis, Sjogren's syndrome, asthma, psoriasis, allergy, diabetes, cardiovascular diseases, arteriosclerosis, restenosis, tumor proliferation, tumor metastasis or rejection in transplantation. Thus, 3-iodo-4-methoxy-1-methyl-2(1H)-quinoline was coupled with (2S)-2-(tert-butoxycarbonylamino)-3-[4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl]propanoic acid Me ester in the presence of PdCl2(dppf) in a mixture of aqueous 2 M Na2CO3 solution and DMF at 90° for 30 min to give (2S)-2-(tert-butoxycarbonylamino)-3-[4-(4-methoxy-1-methyl-2-oxo-1,2-dihydro-3-quinolinyl)phenyl]propanoic acid Me ester which was treated with 4 N HCl/dioxane at room temperature for 30 min followed by evaporation of the solvent and N-acylation with 2,6-dichlorobenzoyl chloride in the presence of Et3N in CH2Cl2 to give (2S)-2-[(2,6-dichlorobenzoyl)amino]-3-[4-(4-methoxy-1-methyl-2-oxo-1,2-dihydro-3-quinolinyl)phenyl]propanoic acid Me ester (II). Saponification of II with LiOH in mixture of THF, H2O, and MeOH followed by purification using reversed phase HPLC gave (2S)-2-[(2,6-dichlorobenzoyl)amino]-3-[4-(4-methoxy-1-methyl-2-oxo-1,2-dihydro-3-quinolinyl)phenyl]propanoic acid (III). III in vitro showed IC50 of 3.5 and 44 nM for inhibiting the binding of recombinant human VCAM-1 to human T cell (Jurkat cell) expressing human integrin $\alpha 4\beta 1$ and that to human B cell lymphoma (RPMI-8866 cell) expressing integrin $\alpha 4\beta 7$, resp.

IT 554418-08-5P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of novel phenylalanine derivs. as $\alpha 4$ integrin inhibitors for treatment or prevention of inflammatory diseases)

IT 554418-04-1P 554418-05-2P 554418-07-4P

554418-10-9P 554418-12-1P 554418-14-3P
 554418-17-6P 554418-19-8P 554418-20-1P
 554418-21-2P 554418-22-3P 554418-23-4P
 554418-24-5P 554418-25-6P 554418-26-7P
 554418-27-8P 554418-35-8P 554418-36-9P
 554418-37-0P 554418-38-1P 554418-39-2P
 554418-40-5P 554418-41-6P 554418-42-7P
 554418-43-8P 554418-44-9P 554418-45-0P
 554418-46-1P 554418-47-2P 554418-48-3P
 554418-49-4P 554418-50-7P 554418-51-8P
 554418-52-9P 554418-55-2P 554418-56-3P
 554418-57-4P 554418-58-5P 554418-59-6P
 554418-60-9P 554418-62-1P 554418-63-2P
 554418-64-3P 554418-65-4P 554418-66-5P
 554418-67-6P 554418-68-7P 554418-69-8P
 554418-70-1P 554418-71-2P 554418-72-3P
 554418-73-4P 554418-74-5P 554418-75-6P
 554418-76-7P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
 (Uses)

(preparation of novel phenylalanine derivs. as $\alpha 4$ integrin inhibitors
 for treatment or prevention of inflammatory diseases)

IT 554418-83-6P 554418-86-9P 554418-97-2P

554418-99-4P 554419-01-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)

(preparation of novel phenylalanine derivs. as $\alpha 4$ integrin inhibitors
 for treatment or prevention of inflammatory diseases)

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:435046 HCAPLUS

DOCUMENT NUMBER: 135:33647

TITLE: Preparation of pyridinyl phenylalanine derivatives

INVENTOR(S): Kaplan, Gerald Lewis; Sidduri, Achyutharao; Tilley,
 Jefferson Wright

PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.

SOURCE: PCT Int. Appl., 97 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001042215	A1	20010614	WO 2000-EP11979	20001129
W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
US 6388084	B1	20020514	US 2000-717684	20001121
BR 2000016172	A	20020820	BR 2000-16172	20001129
EP 1244625	A1	20021002	EP 2000-985117	20001129
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			

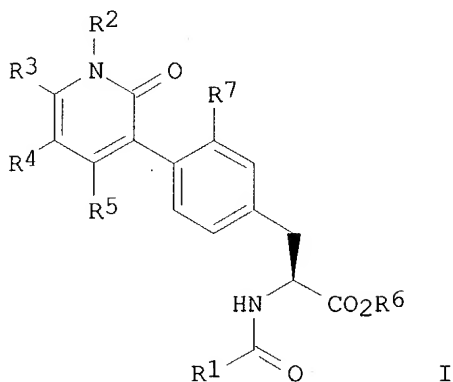
JP 2003516392	T2	20030513	JP 2001-543516	20001129
NZ 518888	A	20040227	NZ 2000-518888	20001129
US 2002133015	A1	20020919	US 2002-59618	20020129
NO 2002002650	A	20020605	NO 2002-2650	20020605

PRIORITY APPLN. INFO.:

US 1999-169090P	P	19991206
US 2000-245603P	P	20001103
US 2000-717684	A3	20001121
WO 2000-EP11979	W	20001129

OTHER SOURCE(S): MARPAT 135:33647

GI



AB Pyridinyl phenylalanine derivs. I (R1 = substituted aryl, substituted 5 or 6 membered heteroarom. ring containing N, O and S bonded via a carbon atom to the amide carbonyl, 3-7 membered ring substituted with alkyl, alkenyl, fluorinealkenyl, arylalkyl, heteroarylalkyl, azidoalkyl, cyanoalkyl, hydroxyalkyl, alkyl sulfonyl, alkyl sulfinyl; R2 = H, (un)substituted alkyl, aryl, or arylalkyl; R3 = H, halogen, alkyl, trifluoromethyl, or aryl; R4 = H, halogen, alkyl, or aryl; R5 = H, alkyl, alkoxy, trifluoromethyl, or aryl; R6 = H, alkyl, alkylcarbonyloxy, substituted aminoalkyl, substituted heterocyclylalkyl; R7 = H, Cl, alkoxy, or alkyl) were prepared as inhibitors of the binding of VCAM-1 to VLA-4 and are useful in treating chronic inflammatory diseases. Thus, N-[(2-chloro-6-methylphenyl)carbonyl]-4-(5-chloro-1-methyl-2-oxo-3-pyridinyl)-L-phenylalanine (II) was prepared from N-[(1,1-dimethylethoxy)carbonyl]-4-iodo-L-phenylalanine Me ester in 5 steps via palladium catalyzed reaction with 3-bromo-5-chloro-1-methyl-2-pyridinone and coupling with 2-chloro-6-methylbenzoic acid. II showed antiinflammatory activity in vitro in the VCAM/VLA-4 screening assay (IC50 < 1 nM).

IT 343981-05-5P 343981-06-6P 343981-07-7P
 343981-08-8P 343981-12-4P 343981-13-5P
 343981-14-6P 343981-18-0P 343981-23-7P
 343981-25-9P 343981-32-8P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of pyridinyl phenylalanine derivs. as anti-inflammatory agents)

IT 343981-15-7P 343981-20-4P 343981-24-8P
 343981-26-0P 343981-27-1P 343981-28-2P
 343981-29-3P 343981-30-6P 343981-31-7P
 343981-33-9P 343981-35-1P 343981-36-2P
 343981-37-3P 343981-38-4P 343981-39-5P
 343981-40-8P 343981-41-9P 343981-42-0P
 343981-43-1P 343981-44-2P 343981-45-3P
 343981-46-4P 343981-47-5P 343981-48-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyridinyl phenylalanine derivs. as anti-inflammatory agents)

IT 343981-54-4P 343981-55-5P 343981-60-2P
343981-61-3P 343981-64-6P 343981-70-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of pyridinyl phenylalanine derivs. as anti-inflammatory agents)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:513663 HCAPLUS

DOCUMENT NUMBER: 133:120678

TITLE: Preparation of amino acid multicyclic derivatives as inhibitors of leukocyte adhesion mediated by VLA-4

INVENTOR(S): Grant, Francine S.; Johnson, Bradley S.; Pleiss, Michael A.; Thorsett, Eugene D.

PATENT ASSIGNEE(S): Elan Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 138 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000043354	A2	20000727	WO 2000-US1604	20000121
WO 2000043354	A3	20001123		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2357781	AA	20000727	CA 2000-2357781	20000121
------------	----	----------	-----------------	----------

EP 1144364	A2	20011017	EP 2000-911619	20000121
------------	----	----------	----------------	----------

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

US 6465513	B1	20021015	US 2000-489157	20000121
------------	----	----------	----------------	----------

US 2003134874	A1	20030717	US 2002-243731	20020916
---------------	----	----------	----------------	----------

PRIORITY APPLN. INFO.: US 1999-116735P A2 19990122

US 1999-117743P A2 19990129

US 2000-489157 A1 20000121

WO 2000-US1604 W 20000121

OTHER SOURCE(S): MARPAT 133:120678

AB Disclosed are compds. A-CONR3CR1R2X1 [A is an optionally substituted multicyclic bridged cycloalkyl, cycloalkenyl, or heterocyclic group that does not contain a lactam; R1 = (CH2)x-Ar-O-Z-R4, Ar1-Ar2-C1-10alkyl, -C2-10alkenyl, or -C2-10alkynyl where Ar, Ar1, Ar2 = (un)substituted aryl or heteroaryl, Z = CO, SO2; R4 = amino or heterocyclic group; x = 1-4; R2 = H, (un)substituted alkyl, alkenyl, alkynyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl; R3 = H or (un)substituted alkyl; X1 = CO2H, P(O)(OH)2, P(O)H(OH), SO2H, SO3H, CONH2 or their esters or derivs., or 5-tetrazolyl] which bind VLA-4. Thus, N-(3-carboxyadamant-1-ylcarbonyl)-4-(2'-cyanophenyl)-L-phenylalanine was prepared by a seven-step procedure involving coupling of 4-(2'-cyanophenyl)-L-phenylalanine Me ester trifluoroacetate salt with (3-methoxycarbonyl)-1-adamantanecarboxylic

acid, followed by saponification
IT 284688-87-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation of amino acid multicyclic derivs. as inhibitors of leukocyte
adhesion mediated by VLA-4)
IT 284689-04-9P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
study); PREP (Preparation); USES (Uses)
(preparation of amino acid multicyclic derivs. as inhibitors of leukocyte
adhesion mediated by VLA-4)

=>
=>

=> fil caold
FILE 'CAOLD' ENTERED AT 18:08:03 ON 21 JUN 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1907-1966
FILE LAST UPDATED: 01 May 1997 (19970501/UP)

This file contains CAS Registry Numbers for easy and accurate
substance identification. Title keywords, authors, patent
assignees, and patent information, e.g., patent numbers, are
now searchable from 1907-1966. TIFF images of CA abstracts
printed between 1907-1966 are available in the PAGE
display formats.

This file supports REGISTRY for direct browsing and searching of
all substance data from the REGISTRY file. Enter HELP FIRST for
more information.

=>
=>

=> => s 127
L29 0 L27

=>
=>

=> fil reg
FILE 'REGISTRY' ENTERED AT 18:08:16 ON 21 JUN 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2004 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES: 20 JUN 2004 HIGHEST RN 696584-79-9
DICTIONARY FILE UPDATES: 20 JUN 2004 HIGHEST RN 696584-79-9

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
<http://www.cas.org/ONLINE/DBSS/registryss.html>

=>

=>

=> d reg 127 tot

1	RN	554419-01-1	REGISTRY
2	RN	554418-99-4	REGISTRY
3	RN	554418-97-2	REGISTRY
4	RN	554418-86-9	REGISTRY
5	RN	554418-83-6	REGISTRY
6	RN	554418-76-7	REGISTRY
7	RN	554418-75-6	REGISTRY
8	RN	554418-74-5	REGISTRY
9	RN	554418-73-4	REGISTRY
10	RN	554418-72-3	REGISTRY
11	RN	554418-71-2	REGISTRY
12	RN	554418-70-1	REGISTRY
13	RN	554418-69-8	REGISTRY
14	RN	554418-68-7	REGISTRY
15	RN	554418-67-6	REGISTRY
16	RN	554418-66-5	REGISTRY
17	RN	554418-65-4	REGISTRY
18	RN	554418-64-3	REGISTRY
19	RN	554418-63-2	REGISTRY
20	RN	554418-62-1	REGISTRY
21	RN	554418-60-9	REGISTRY
22	RN	554418-59-6	REGISTRY
23	RN	554418-58-5	REGISTRY
24	RN	554418-57-4	REGISTRY
25	RN	554418-56-3	REGISTRY
26	RN	554418-55-2	REGISTRY
27	RN	554418-52-9	REGISTRY
28	RN	554418-51-8	REGISTRY
29	RN	554418-50-7	REGISTRY
30	RN	554418-49-4	REGISTRY
31	RN	554418-48-3	REGISTRY
32	RN	554418-47-2	REGISTRY
33	RN	554418-46-1	REGISTRY
34	RN	554418-45-0	REGISTRY
35	RN	554418-44-9	REGISTRY
36	RN	554418-43-8	REGISTRY
37	RN	554418-42-7	REGISTRY
38	RN	554418-41-6	REGISTRY
39	RN	554418-40-5	REGISTRY
40	RN	554418-39-2	REGISTRY
41	RN	554418-38-1	REGISTRY
42	RN	554418-37-0	REGISTRY
43	RN	554418-36-9	REGISTRY
44	RN	554418-35-8	REGISTRY
45	RN	554418-27-8	REGISTRY
46	RN	554418-26-7	REGISTRY
47	RN	554418-25-6	REGISTRY
48	RN	554418-24-5	REGISTRY
49	RN	554418-23-4	REGISTRY
50	RN	554418-22-3	REGISTRY
51	RN	554418-21-2	REGISTRY
52	RN	554418-20-1	REGISTRY
53	RN	554418-19-8	REGISTRY

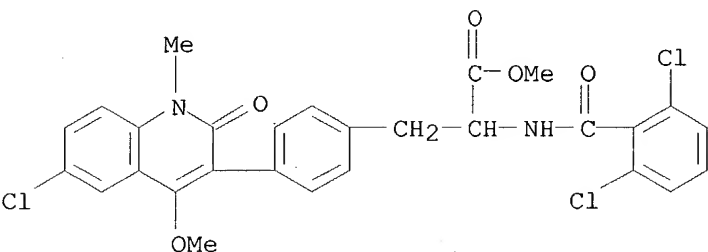
54	RN	554418-17-6	REGISTRY
55	RN	554418-14-3	REGISTRY
56	RN	554418-12-1	REGISTRY
57	RN	554418-10-9	REGISTRY
58	RN	554418-08-5	REGISTRY
59	RN	554418-07-4	REGISTRY
60	RN	554418-05-2	REGISTRY
61	RN	554418-04-1	REGISTRY
62	RN	343981-70-4	REGISTRY
63	RN	343981-64-6	REGISTRY
64	RN	343981-61-3	REGISTRY
65	RN	343981-60-2	REGISTRY
66	RN	343981-55-5	REGISTRY
67	RN	343981-54-4	REGISTRY
68	RN	343981-48-6	REGISTRY
69	RN	343981-47-5	REGISTRY
70	RN	343981-46-4	REGISTRY
71	RN	343981-45-3	REGISTRY
72	RN	343981-44-2	REGISTRY
73	RN	343981-43-1	REGISTRY
74	RN	343981-42-0	REGISTRY
75	RN	343981-41-9	REGISTRY
76	RN	343981-40-8	REGISTRY
77	RN	343981-39-5	REGISTRY
78	RN	343981-38-4	REGISTRY
79	RN	343981-37-3	REGISTRY
80	RN	343981-36-2	REGISTRY
81	RN	343981-35-1	REGISTRY
82	RN	343981-33-9	REGISTRY
83	RN	343981-32-8	REGISTRY
84	RN	343981-31-7	REGISTRY
85	RN	343981-30-6	REGISTRY
86	RN	343981-29-3	REGISTRY
87	RN	343981-28-2	REGISTRY
88	RN	343981-27-1	REGISTRY
89	RN	343981-26-0	REGISTRY
90	RN	343981-25-9	REGISTRY
91	RN	343981-24-8	REGISTRY
92	RN	343981-23-7	REGISTRY
93	RN	343981-20-4	REGISTRY
94	RN	343981-18-0	REGISTRY
95	RN	343981-15-7	REGISTRY
96	RN	343981-14-6	REGISTRY
97	RN	343981-13-5	REGISTRY
98	RN	343981-12-4	REGISTRY
99	RN	343981-08-8	REGISTRY
100	RN	343981-07-7	REGISTRY
101	RN	343981-06-6	REGISTRY
102	RN	343981-05-5	REGISTRY
103	RN	284689-04-9	REGISTRY
104	RN	284688-87-5	REGISTRY

=> d ide can 127 1 5 10 15 20 25 30 35 40 45 50 55 60 65 70 75 80 85 90 95 100 104

L27 ANSWER 1 OF 104 REGISTRY COPYRIGHT 2004 ACS on STN
 RN 554419-01-1 REGISTRY
 CN Phenylalanine, 4-(6-chloro-1,2-dihydro-4-methoxy-1-methyl-2-oxo-3-quinolinyl)-N-(2,6-dichlorobenzoyl)-, methyl ester (9CI) (CA INDEX NAME)
 FS 3D CONCORD
 MF C28 H23 Cl3 N2 O5
 SR CA
 LC STN Files: CA, CAPLUS, TOXCENTER

DT.CA CAPLUS document type: Patent

RL.P Roles from patents: PREP (Preparation); RACT (Reactant or reagent)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:85646

L27 ANSWER 5 OF 104 REGISTRY COPYRIGHT 2004 ACS on STN

RN 554418-83-6 REGISTRY

CN L-Phenylalanine, N-(2,6-dichlorobenzoyl)-4-(1,2-dihydro-1-methyl-2-oxo-3-quinolinyl)-, methyl ester (9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C27 H22 Cl2 N2 O4

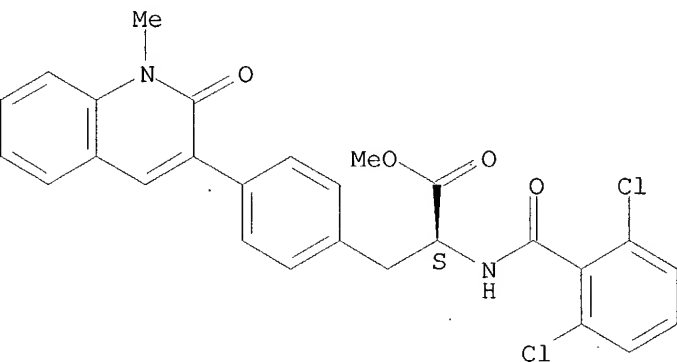
SR CA

LC STN Files: CA, CAPLUS, TOXCENTER

DT.CA CAPLUS document type: Patent

RL.P Roles from patents: PREP (Preparation); RACT (Reactant or reagent)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:85646

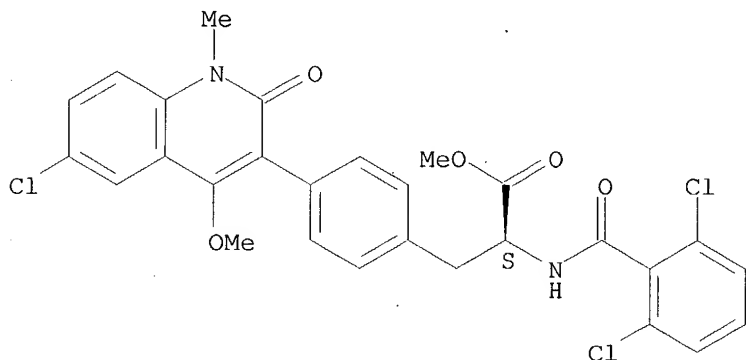
L27 ANSWER 10 OF 104 REGISTRY COPYRIGHT 2004 ACS on STN

RN 554418-72-3 REGISTRY

CN L-Phenylalanine, 4-(6-chloro-1,2-dihydro-4-methoxy-1-methyl-2-oxo-3-quinolinyl)-N-(2,6-dichlorobenzoyl)-, methyl ester (9CI) (CA INDEX NAME)

FS STEREOSEARCH
 MF C28 H23 Cl3 N2 O5
 SR CA
 LC STN Files: CA, CAPLUS, TOXCENTER
 DT.CA Caplus document type: Patent
 RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.



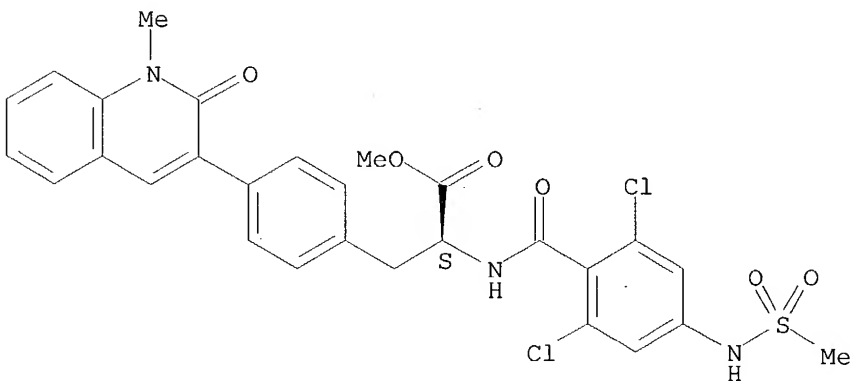
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:85646

L27 ANSWER 15 OF 104 REGISTRY COPYRIGHT 2004 ACS on STN
 VRN 554418-67-6 REGISTRY
 CN L-Phenylalanine, N-[2,6-dichloro-4-[(methylsulfonyl)amino]benzoyl]-4-(1,2-dihydro-1-methyl-2-oxo-3-quinolinyl)-, methyl ester (9CI) (CA INDEX NAME)
 FS STEREOSEARCH
 MF C28 H25 Cl2 N3 O6 S
 SR CA
 LC STN Files: CA, CAPLUS, TOXCENTER
 DT.CA Caplus document type: Patent
 RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.



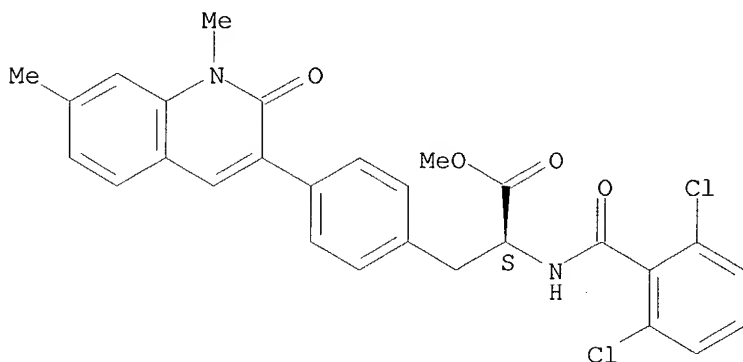
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:85646

L27 ANSWER 20 OF 104 REGISTRY COPYRIGHT 2004 ACS on STN
RN 554418-62-1 REGISTRY
CN L-Phenylalanine, N-(2,6-dichlorobenzoyl)-4-(1,2-dihydro-1,7-dimethyl-2-oxo-3-quinolinyl)-, methyl ester (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C28 H24 Cl2 N2 O4
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER
DT.CA Caplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.



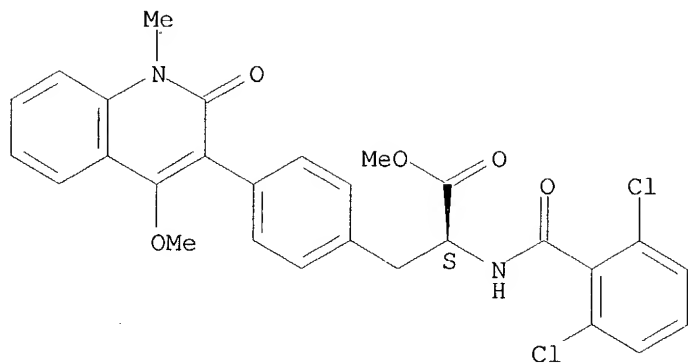
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:85646

L27 ANSWER 25 OF 104 REGISTRY COPYRIGHT 2004 ACS on STN
RN 554418-56-3 REGISTRY
CN L-Phenylalanine, N-(2,6-dichlorobenzoyl)-4-(1,2-dihydro-4-methoxy-1-methyl-2-oxo-3-quinolinyl)-, methyl ester (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C28 H24 Cl2 N2 O5
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER
DT.CA Caplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.



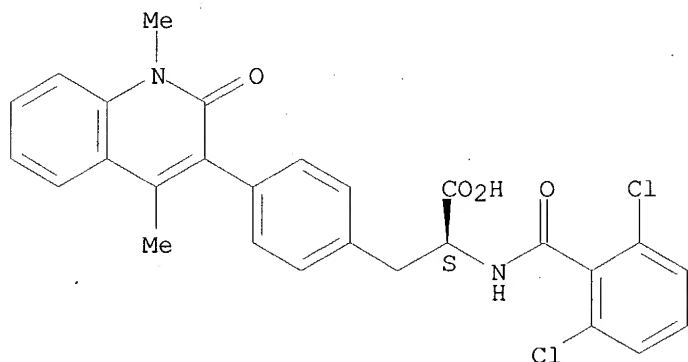
PROPERTY DATA AVAILABLE IN THE 'PROP'.FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:85646

L27 ANSWER 30 OF 104 REGISTRY COPYRIGHT 2004 ACS on STN
RN 554418-49-4 REGISTRY
CN L-Phenylalanine, N-(2,6-dichlorobenzoyl)-4-(1,2-dihydro-1,4-dimethyl-2-oxo-3-quinolinyl)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C27 H22 Cl2 N2 O4
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER
DT.CA Caplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

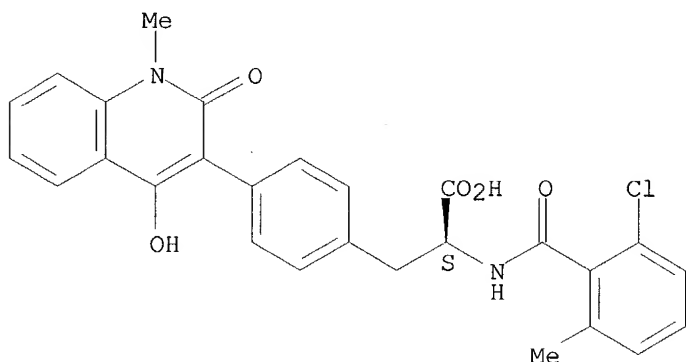
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:85646

L27 ANSWER 35 OF 104 REGISTRY COPYRIGHT 2004 ACS on STN
RN 554418-44-9 REGISTRY

CN L-Phenylalanine, N-(2-chloro-6-methylbenzoyl)-4-(1,2-dihydro-4-hydroxy-1-methyl-2-oxo-3-quinolinyl)- (9CI) (CA INDEX NAME)
 FS STEREOSEARCH
 MF C27 H23 Cl N2 O5
 SR CA
 LC STN Files: CA, CAPLUS, TOXCENTER
 DT.CA Caplus document type: Patent
 RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.



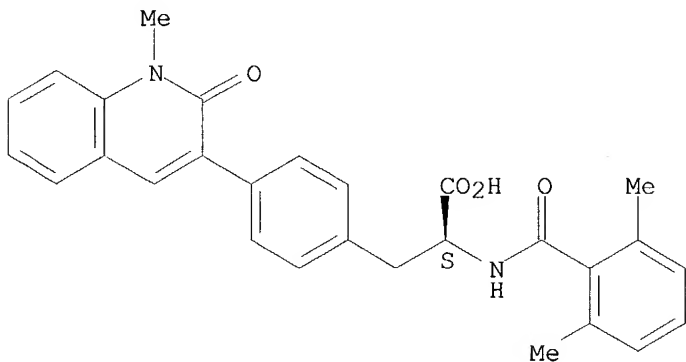
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:85646

L27 ANSWER 40 OF 104 REGISTRY COPYRIGHT 2004 ACS on STN
 RN 554418-39-2 REGISTRY
 CN L-Phenylalanine, 4-(1,2-dihydro-1-methyl-2-oxo-3-quinolinyl)-N-(2,6-dimethylbenzoyl)- (9CI) (CA INDEX NAME)
 FS STEREOSEARCH
 MF C28 H26 N2 O4
 SR CA
 LC STN Files: CA, CAPLUS, TOXCENTER
 DT.CA Caplus document type: Patent
 RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.



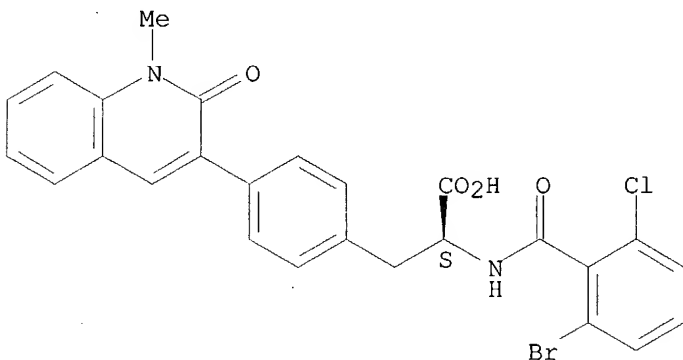
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:85646

L27 ANSWER 45 OF 104 REGISTRY COPYRIGHT 2004 ACS on STN
RN 554418-27-8 REGISTRY
CN L-Phenylalanine, N-(2-bromo-6-chlorobenzoyl)-4-(1,2-dihydro-1-methyl-2-oxo-3-quinolinyl)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C26 H20 Br Cl N2 O4
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.



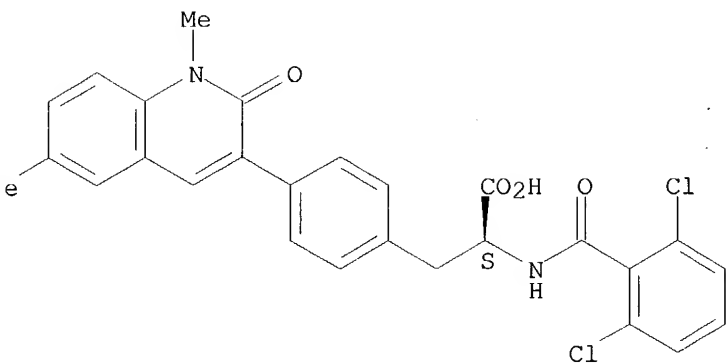
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:85646

L27 ANSWER 50 OF 104 REGISTRY COPYRIGHT 2004 ACS on STN
RN 554418-22-3 REGISTRY
CN L-Phenylalanine, N-(2,6-dichlorobenzoyl)-4-(1,2-dihydro-1,6-dimethyl-2-oxo-3-quinolinyl)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C27 H22 Cl2 N2 O4
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.



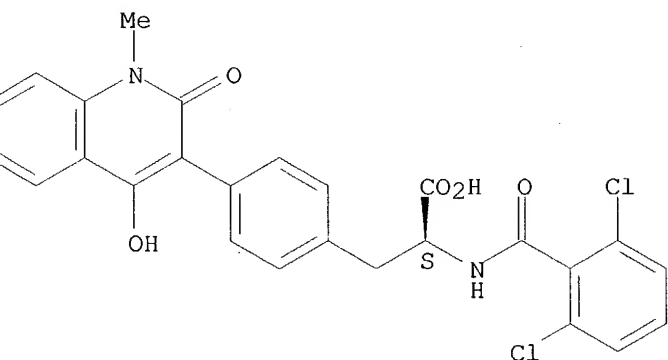
*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:85646

27 ANSWER 55 OF 104. REGISTRY COPYRIGHT 2004 ACS on STN
N 554418-14-3 REGISTRY
N L-Phenylalanine, N-(2,6-dichlorobenzoyl)-4-(1,2-dihydro-4-hydroxy-1-methyl-
2-oxo-3-quinolinyl)- (9CI) (CA INDEX NAME)
S STEREOSEARCH
IF C26 H20 Cl2 N2 O5
R CA
C STN Files: CA, CAPLUS, TOXCENTER
T.CA CAplus document type: Patent
L.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES
(Uses)

absolute stereochemistry.



*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

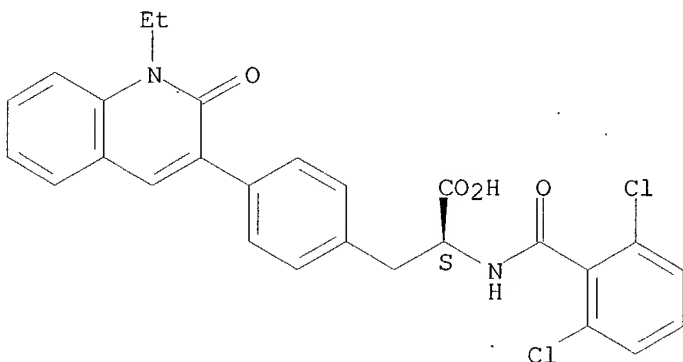
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:85646

27 ANSWER 60 OF 104. REGISTRY COPYRIGHT 2004 ACS on STN
N 554418-05-2 REGISTRY

CN L-Phenylalanine, N-(2,6-dichlorobenzoyl)-4-(1-ethyl-1,2-dihydro-2-oxo-3-quinolinyl)- (9CI) (CA INDEX NAME)
 FS STEREOSEARCH
 MF C27 H22 Cl2 N2 O4
 SR CA
 LC STN Files: CA, CAPLUS, TOXCENTER
 DT.CA Caplus document type: Patent
 RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.



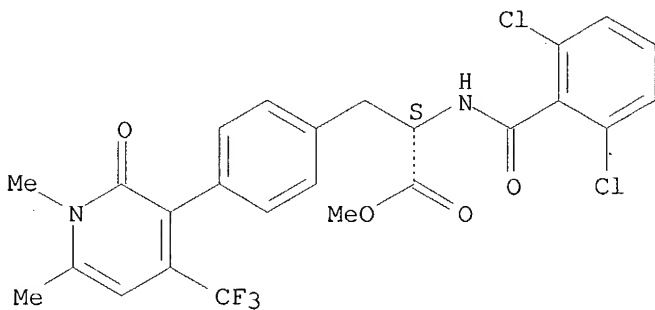
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:85646

L27 ANSWER 65 OF 104 REGISTRY COPYRIGHT 2004 ACS on STN
 RN 343981-60-2 REGISTRY
 CN L-Phenylalanine, N-(2,6-dichlorobenzoyl)-4-[1,2-dihydro-1,6-dimethyl-2-oxo-4-(trifluoromethyl)-3-pyridinyl]-, methyl ester (9CI) (CA INDEX NAME)
 FS STEREOSEARCH
 MF C25 H21 Cl2 F3 N2 O4
 SR CA
 LC STN Files: CA, CAPLUS, USPATFULL
 DT.CA Caplus document type: Patent
 RL.P Roles from patents: PREP (Preparation); RACT (Reactant or reagent)

Absolute stereochemistry.



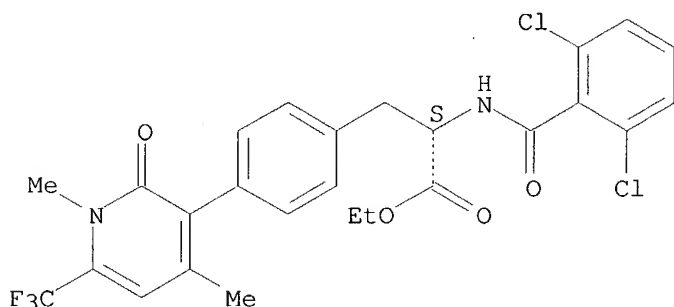
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 135:33647

L27 ANSWER 70 OF 104 REGISTRY COPYRIGHT 2004 ACS on STN
RN 343981-46-4 REGISTRY
CN L-Phenylalanine, N-(2,6-dichlorobenzoyl)-4-[1,2-dihydro-1,4-dimethyl-2-oxo-6-(trifluoromethyl)-3-pyridinyl]-, ethyl ester (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C26 H23 Cl2 F3 N2 O4
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA Caplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.



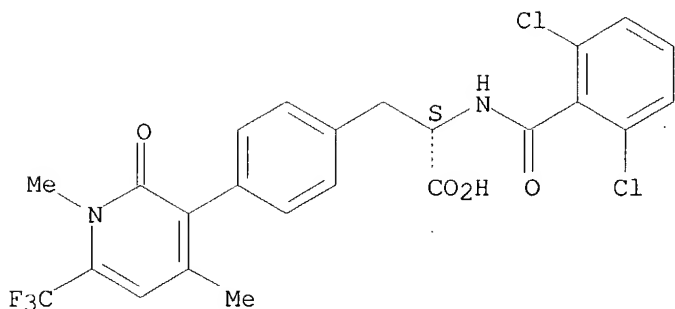
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 135:33647

L27 ANSWER 75 OF 104 REGISTRY COPYRIGHT 2004 ACS on STN
RN 343981-41-9 REGISTRY
CN L-Phenylalanine, N-(2,6-dichlorobenzoyl)-4-[1,2-dihydro-1,4-dimethyl-2-oxo-6-(trifluoromethyl)-3-pyridinyl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C24 H19 Cl2 F3 N2 O4
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA Caplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.



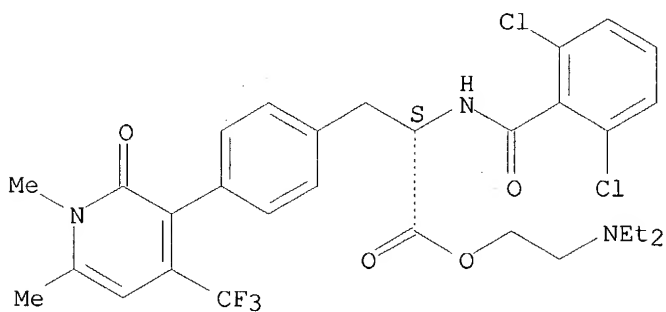
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 135:33647

L27 ANSWER 80 OF 104 REGISTRY COPYRIGHT 2004 ACS on STN
RN 343981-36-2 REGISTRY
CN L-Phenylalanine, N-(2,6-dichlorobenzoyl)-4-[1,2-dihydro-1,6-dimethyl-2-oxo-4-(trifluoromethyl)-3-pyridinyl]-, 2-(diethylamino)ethyl ester (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C30 H32 Cl2 F3 N3 O4
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

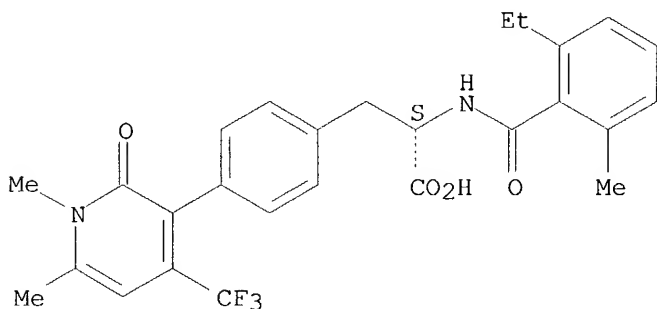
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 135:33647

L27 ANSWER 85 OF 104 REGISTRY COPYRIGHT 2004 ACS on STN
RN 343981-30-6 REGISTRY
CN L-Phenylalanine, 4-[1,2-dihydro-1,6-dimethyl-2-oxo-4-(trifluoromethyl)-3-pyridinyl]-N-(2-ethyl-6-methylbenzoyl)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH

MF C27 H27 F3 N2 O4
 SR CA
 LC STN Files: CA, CAPLUS, USPATFULL
 DT.CA CAplus document type: Patent
 RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.



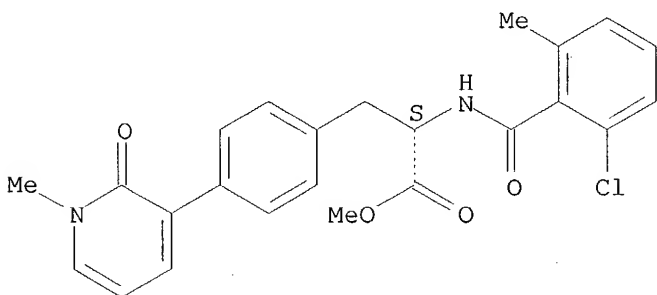
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 135:33647

L27 ANSWER 90 OF 104 REGISTRY COPYRIGHT 2004 ACS on STN
 RN 343981-25-9 REGISTRY
 CN L-Phenylalanine, N-(2-chloro-6-methylbenzoyl)-4-(1,2-dihydro-1-methyl-2-oxo-3-pyridinyl)-, methyl ester (9CI) (CA INDEX NAME)
 FS STEREOSEARCH
 MF C24 H23 Cl N2 O4
 SR CA
 LC STN Files: CA, CAPLUS, USPATFULL
 DT.CA CAplus document type: Patent
 RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

Absolute stereochemistry.



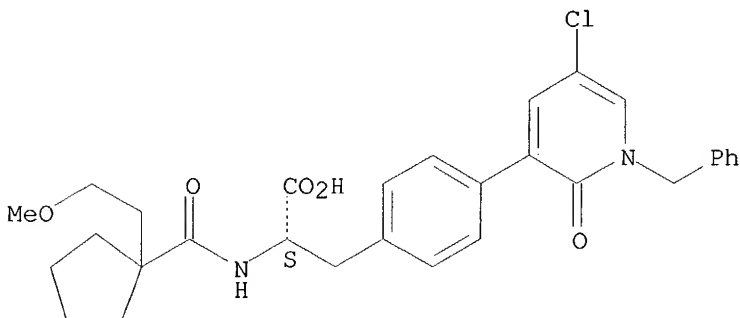
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 135:33647

L27 ANSWER 95 OF 104 REGISTRY COPYRIGHT 2004 ACS on STN
 RN 343981-15-7 REGISTRY
 CN L-Phenylalanine, 4-[5-chloro-1,2-dihydro-2-oxo-1-(phenylmethyl)-3-pyridinyl]-N-[[1-(2-methoxyethyl)cyclopentyl]carbonyl]- (9CI) (CA INDEX NAME)
 FS STEREOSEARCH
 MF C30 H33 Cl N2 O5
 SR CA
 LC STN Files: CA, CAPLUS, USPATFULL
 DT.CA Caplus document type: Patent
 RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.



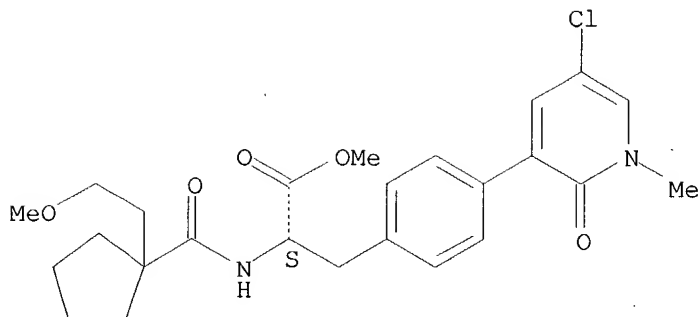
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 135:33647

L27 ANSWER 100 OF 104 REGISTRY COPYRIGHT 2004 ACS on STN
 RN 343981-07-7 REGISTRY
 CN L-Phenylalanine, 4-(5-chloro-1,2-dihydro-1-methyl-2-oxo-3-pyridinyl)-N-[[1-(2-methoxyethyl)cyclopentyl]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)
 FS STEREOSEARCH
 MF C25 H31 Cl N2 O5
 SR CA
 LC STN Files: CA, CAPLUS, USPATFULL
 DT.CA Caplus document type: Patent
 RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

Absolute stereochemistry.



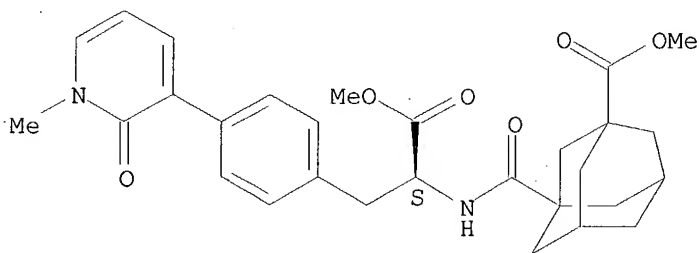
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 135:33647

L27 ANSWER 104 OF 104 REGISTRY COPYRIGHT 2004 ACS on STN
RN 284688-87-5 REGISTRY
CN Tricyclo[3.3.1.1^{3,7}]decane-1-carboxylic acid, 3-[[[(1S)-1-[[4-(1,2-dihydro-1-methyl-2-oxo-3-pyridinyl)phenyl]methyl]-2-methoxy-2-oxoethyl]amino]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C29 H34 N2 O6
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA Caplus document type: Patent
RL.P Roles from patents: PREP (Preparation); RACT (Reactant or reagent)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 133:120678

=>